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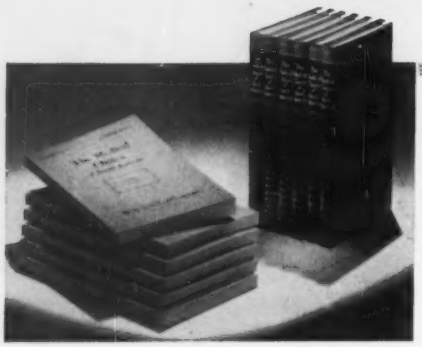

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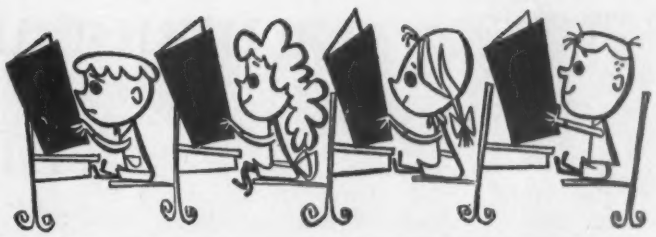

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Few emergencies are remembered as vividly as those of sudden cessation of cardiac output—and more cases appear during the first ten years of life than in any other decade. This remarkable percentage—almost one-fourth of all cases—makes it imperative that general practitioners and pediatricians concern themselves with both the prevention and treatment of cardiac arrest.

A truly complete monograph on the subject, CARDIAC ARREST AND RESUSCITATION by Dr. Hugh E. Stephenson, Jr. contains in one volume an accumulation of all the information currently available on the subject—historical information, research data and practical considerations. This valuable new book can help you to further understand the problems involved in cardiac arrest and resuscitation and can acquaint you with all the facts necessary to successfully resuscitate a human heart. Many of the conclusions presented are based on a study of more than 1,700 cases contained in the Cardiac Arrest Registry established by the author with the cooperation of physicians all over the world. You'll find this new book contains a wealth of useful information that will prepare you for that moment when you might have to resuscitate a human heart—and save a human life.

By HUGH E. STEPHENSON, JR., M.D., Professor and Chairman, Department of Surgery, University of Missouri School of Medicine; Chief of Surgical Service, University of Missouri Hospitals. New. 1958, 378 pages, 6¾" x 9¼", 31 illustrations. Price, $12.00.

C V M

The C. V. Mosby Company
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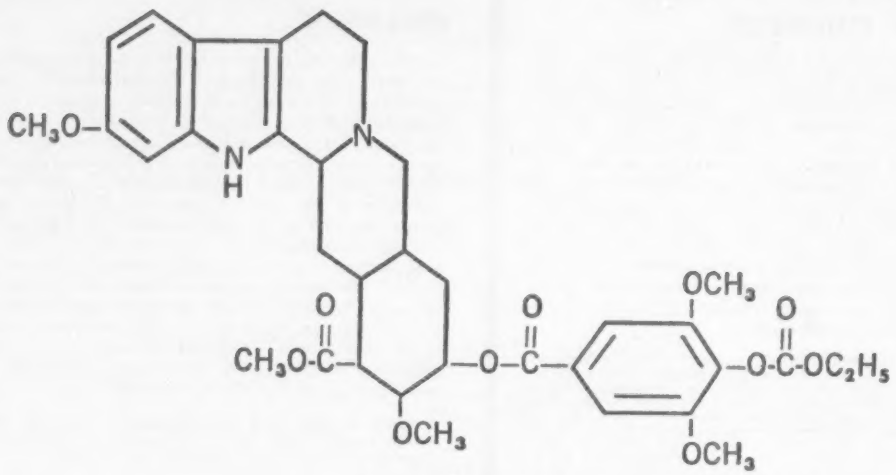
a major improvement in rauwolfia... a major advance in antihypertensive therapy



Created in the laboratory by altering the reserpine molecule so as to preserve an antihypertensive effect and minimize undesirable side actions.

Singoserp™

Dosage: In new patients: Average initial dose, 1 to 2 tablets (1 to 2 mg.) daily. Some patients may require and will tolerate 3 or more tablets daily. Maintenance dose will range from ½ to 3 tablets (0.5 to 3 mg.) daily. When necessary for adequate control of blood pressure, more potent agents may be used adjunctively with Singoserp in doses below those required when they are used alone.

In patients taking other antihypertensive medication:
Add 1 to 2 Singoserp tablets (1 to 2 mg.) daily. Dosage of other agents should be revised downward to a level affording maximal control of blood pressure and minimal side effects.

Supplied: Singoserp *Tablets,* 1 mg. (white, scored); bottles of 100.

Singoserp™

(syrosingopine CIBA)

Minimizes the side effects problem in most hypertensive patients

1. For new hypertensive patients Singoserp is a useful antihypertensive drug for new patients because it often lowers blood pressure with less of the side effects problem posed by conventional rauwolfia agents.

2. For hypertensive patients already undergoing drug treatment Singoserp, added to any antihypertensive regimen, frequently makes it possible to maintain blood pressure levels achieved with more potent agents, while reducing their dosage requirements.

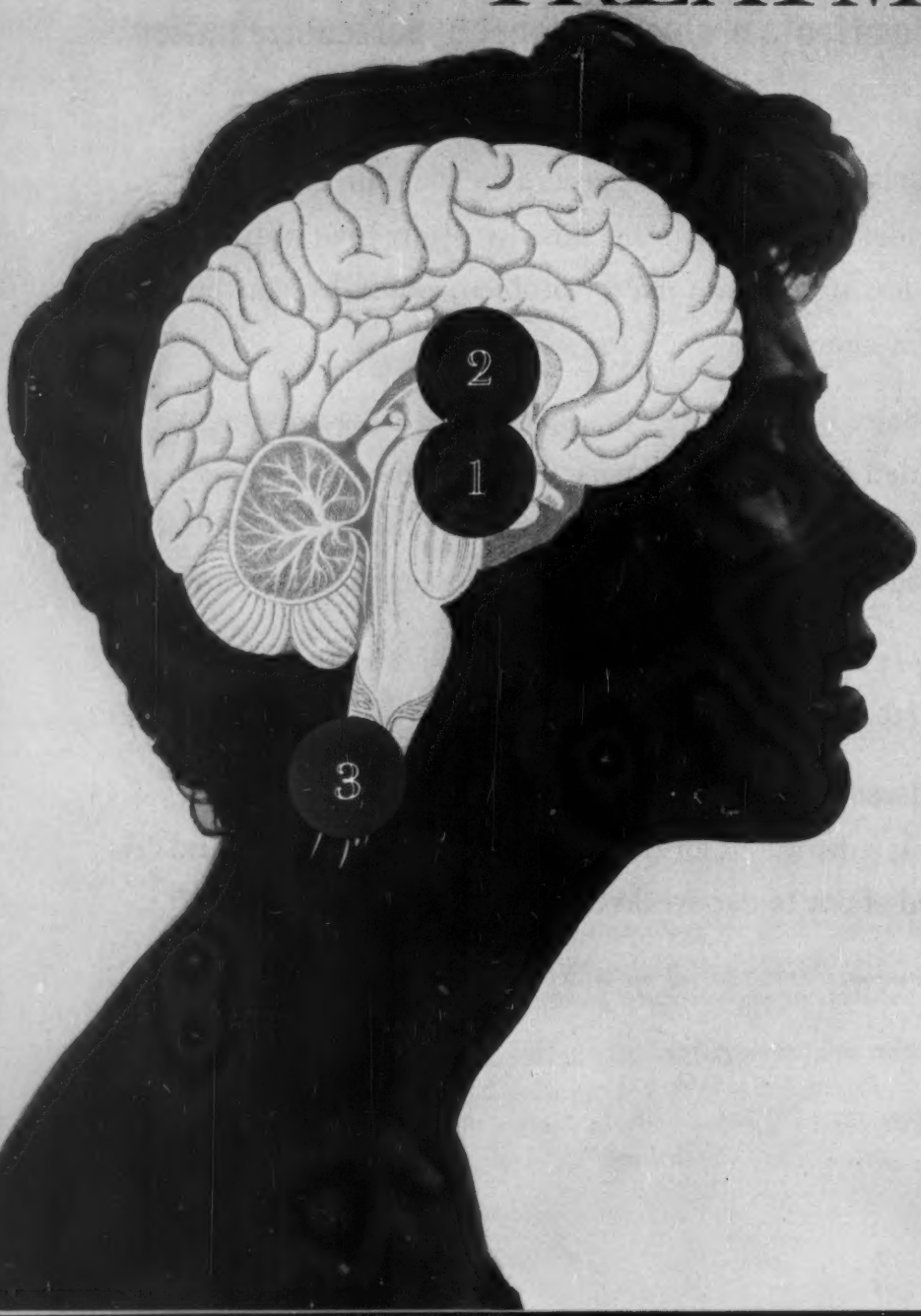
Less sedation—"It [Singoserp] is . . . definitely less sedative or tranquilizing [than reserpine]."[1]

Depression relieved—"In those patients who had been depressed, [Singoserp] was substituted for other Rauwolfia preparations and within a period of one to two weeks this depression was relieved."[2]

References: 1. Wolffe, J. B.: Mod. Med. *26*:253 (Feb. 1) 1958. 2. Bartels, C. C.: To be published.

CIBA
SUMMIT, N.J.

'Deprol' provides COMPREHENSIVE TREATMENT



at three levels

1
hypothalamus

2
thalamus and limbic system

3
spinal cord

FOR DEPRESSION

AND ASSOCIATED ANXIETY AND PHYSICAL TENSION

"Features of anxiety commonly accompany depressive features, and not infrequently these anxiety symptoms, not those of the underlying and primary depression, are the presenting ones."

Yonge, K.A.: Depressions in disguise. Canad. M.A.J. 74:693, May 1, 1956.

RELIEVES DEPRESSION
by improving mood and outlook without excessive stimulation or rebound depression. Relieves symptoms such as crying, lethargy, loss of appetite, insomnia.

RELIEVES ASSOCIATED ANXIETY
by reducing exaggerated reaction at the seat of emotions. Does not depress cortical activity. Does not impair mental efficiency or normal behavior. No risk of drug-induced depression.

RELIEVES ASSOCIATED PHYSICAL TENSION
by relaxing skeletal muscle. Aids restful sleep and reduces likelihood of symptom formation due to depression. Does not impair motor control.

- Confirmed efficacy
- Documented safety
- Simple q.i.d. dosage

▲Deprol▲†

benactyzine + meprobamate

Supplied: Bottles of 50 light-pink, scored tablets.
Composition: Each tablet contains 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

WALLACE LABORATORIES, *New Brunswick, N. J.*

†TRADE-MARK

69-9109

HIGHLIGHTS FROM THE A.M.A. COUNCIL ON DRUGS

REPORT ON TRIAMCINOLONE

J.A.M.A. 169:257 (January 17) 1959.

'It [triamcinolone] has an anti-inflammatory potency greater than an equal amount of prednisolone; i.e., comparable suppressive effects may usually be achieved with lower doses of triamcinolone than with prednisolone."

"Triamcinolone lacks the sodium-retaining and edema-producing effects of most other glucocorticoids. During the first several days of administration, it may cause a loss of sodium from the body; an initial mild diuretic action is frequently observed, whether the patient is frankly edematous or not. This is in contrast to the definite sodium-retaining and fluid-retaining properties of cortisone and hydrocortisone and to a much lesser extent with prednisone and prednisolone."

"Except in exceedingly large doses, triamcinolone apparently has no consistent effect on potassium excretion. Hence, neither sodium restriction nor potassium supplementation is ordinarily required during therapy with this agent."

"As with other glucocorticoids, the long-term administration of triamcinolone results in definite catabolic effects, as indicated by impairment of carbohydrate utilization and negative protein and calcium balance. This catabolic effect, coupled with a lack of appetite stimulation which is apparently peculiar to triamcinolone, may produce weight loss that might be undesirable in some patients treated for long periods of time."

"...the voracious appetite, with weight gain and euphoria, characteristic of other steroids, is not seen with administration of triamcinolone."

"Triamcinolone has been used for the management of a wide variety of clinical conditions usually considered amenable to systemic steroid therapy. These have included rheumatoid arthritis and other collagen diseases, allergic and dermatological disorders, certain leukemias and malignant lymphomas, the nephrotic syndrome, pulmonary emphysema and fibrosis, acute bursitis, rheumatic fever, and certain blood dyscrasias. Although clinical experience with the drug in some of the foregoing conditions is not extensive, the many similarities in action between triamcinolone and other potent glucocorticoids would indicate a usefulness for triamcinolone akin to that of other agents of this class."

"There is some evidence that triamcinolone is more effective at a smaller dosage than are other steroids in controlling both the skin and joint lesions in psoriasis, whether or not complicated by arthropathy."

"Triamcinolone appears to compare favorably with other steroids for use in those situations in which edema and sodium retention have been complicating problems."

"It [triamcinolone] may also be the steroid of choice for patients in whom psychic stimulation, euphoria, voracious appetite, and weight gain should be avoided."

"... the drug [triamcinolone] does produce the other side effects and untoward reactions common to the glucocorticoids. At therapeutically equivalent doses, the frequency and severity of clinical manifestations of hyperadrenalism — rounding of the face, fat deposition, and hirsutism — are essentially the same. Likewise, there is little indication that the relative incidence of osteoporosis is materially decreased after the long-term use of the drug."

"Triamcinolone apparently does not cause the euphoria sometimes seen with other steroids, and the occurrence of mental depressions is uncommon."

"Current evidence suggests that the drug [triamcinolone] may not produce as high an incidence of peptic ulcer as do other steroids."

"Cutaneous erythema seems to be a side effect peculiar to triamcinolone."

"The usual contraindications and precautions of glucocorticoid therapy should be followed in the use of triamcinolone, keeping in mind that prolonged therapy with this drug will suppress the function of the patient's own adrenals by interfering with the pituitary-adrenal axis."

Aristocort®

Triamcinolone LEDERLE

Supplied: 1 mg. scored tablets (yellow)
2 mg. scored tablets (pink)
4 mg. scored tablets (white)

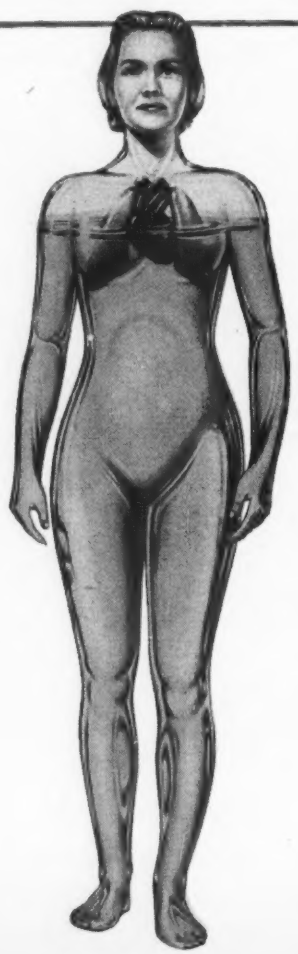
Lederle LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

From basic research—basic progress

A NEW MEASURE OF ACTIVITY

IN EDEMA:

- shows greater oral potency than any other class of diuretic agent
- each 25 mg. HYDRODIURIL orally is equivalent to 1.6 cc. meralluride I.M.
- has been reported to be effective even in certain patients who do not respond satisfactorily to other diuretics.
- has prompt onset of action with diuretic effectiveness maintained even on prolonged daily administration
- low toxicity—extremely well tolerated
- often achieves the benefits of a low salt diet without the unpleasant restriction



INDICATIONS: Hypertension, congestive heart failure of all degrees of severity, premenstrual syndrome (edema), edema and toxemia of pregnancy, renal edema—nephrosis, nephritis; cirrhosis with ascites, drug-induced edema, and as adjunctive therapy in the management of obesity complicated by edema.

DOSAGE: In edema—one or two 50 mg. tablets of HYDRODIURIL once or twice a day.

In hypertension—one or two 25 mg. tablets or one 50 mg. tablet HYDRODIURIL once or twice a day.

SUPPLIED: 25 mg. and 50 mg. scored tablets HYDRODIURIL (Hydrochlorothiazide) in bottles of 100 and 1,000.

*HYDRODIURIL and DIURIL are trademarks of Merck & Co., INC.

Additional information on HYDRODIURIL is available to the physician on request.

BIBLIOGRAPHY: 1 Esch, A. F., Wilson, I. M. and Freis, E. D.: 3,4-Dihydrochlorothiazide: Clinical Evaluation of a New Saluretic Agent. Preliminary Report; M. Ann. District of Columbia 28:9 (Jan.) 1959. 2 Ford, R. V.: The Clinical Pharmacology of Hydrochlorothiazide; Southern Med. J. 52:40 (Jan.) 1959. 3 Fuchs, M., Bodi, T., Irie, S. and Moyer, J. H.: Preliminary Evaluation of Hydrochlorothiazide ('HYDRODIURIL'); M. Rec. & Ann. 51:872, (Dec.) 1958. 4 Moyer, J. H., Fuchs, M., Irie, S. and Bodi, T.: Some Observations on the Pharmacology of Hydrochlorothiazide; Am. J. Cardiol. 3:113, (Jan.) 1959.

HYDRODIURIL (HYDROCHLOROTHIAZIDE)

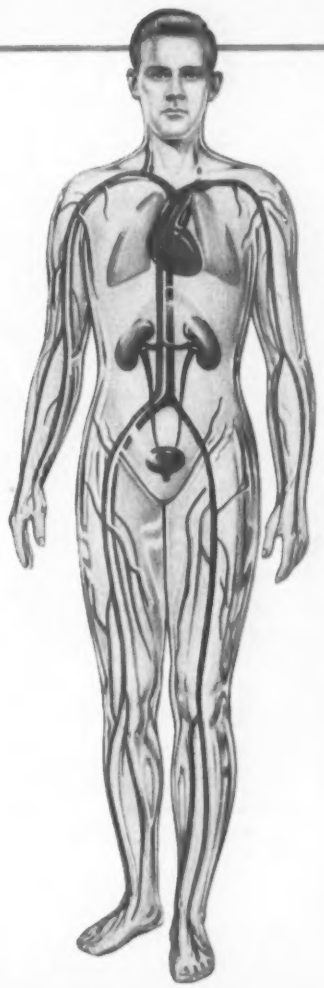
- highly-active derivative of chlorothiazide
- qualitatively similar to DIURIL® but at least 10 to 12 times more potent by weight
- loss of potassium is clinically insignificant in the great majority of patients on normal diets

HYDRODIURIL*

NEW RELEASE

HYDROCHLOROTHIAZIDE

IN HYPERTENSION:



- effective by itself in some patients—markedly potentiates other antihypertensive agents
- provides background therapy to improve and simplify the management of all grades of hypertension
- has been reported by some investigators to have a greater antihypertensive potency in some patients than chlorothiazide at equivalent dosage
- does not lower blood pressure in normotensives
- reduces dosage requirements for other antihypertensive agents, often with concomitant reduction in their distressing side effects
- smooths out blood pressure fluctuations

PRECAUTIONS: It is important that the dosage be adjusted as frequently as the needs of the individual patient demand. When HYDRODIURIL is used with a ganglion blocking agent, it is mandatory to reduce the dose of the latter by at least 50 per cent, immediately upon adding HYDRODIURIL to the regimen.

HYDRODIURIL has shown no adverse effects on renal function; for this reason it may be used with excellent results even in patients for whom the organomercurials are contraindicated because of renal damage.

The excretion of potassium is much lower than that of sodium or chloride and, as is the case with DIURIL®, the loss of potassium is clinically insignificant in the great majority of patients on normal diets. If indicated, potassium loss may easily be replaced by including potassium-rich foods in the diet (orange juice, bananas, etc.).

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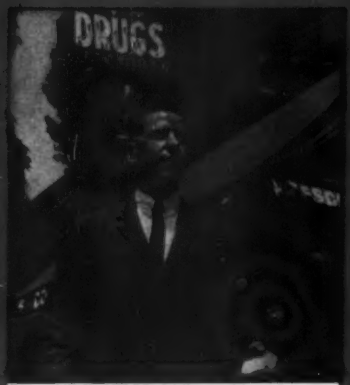
ONE PITCH AND I STRUCK OUT...

Just an hour of pitching baseball with my son and I "threw my arm out." Painful? I couldn't even sleep that night!

Next day on the job I was a total loss—could hardly lift a slide rule!



I saw my doctor that night and got a prescription for some tablets.

Percodan®-Demi & Percodan® Tablets

Salts of Dihydrohydroxycodeinone and Homatropine, plus APC

FOR PAIN

Amazing! The pain went away fast—in about 15 minutes. I slept like a baby. Finished my design for the new warehouse next day, and not a bit of trouble since!

ACTS FAST—usually within 5-15 minutes. **LASTS LONG**—usually 6 hours or more. **THOROUGH RELIEF**—permits uninterrupted sleep through the night. **RARELY CONSTIPATES**—excellent for chronic or bedridden patients. **VERSATILE**—new "demi" strength permits dosage flexibility to meet each patient's specific needs. PERCODAN-DEMI provides the PERCODAN formula with one-half the amount of salts of dihydrohydroxycodeinone and homatropine.

AVERAGE ADULT DOSE: 1 tablet every 6 hours. May be habit-forming. Federal law permits oral prescription.

Each PERCODAN® Tablet contains 4.50 mg. dihydrohydroxycodeinone hydrochloride, 0.38 mg. dihydrohydroxycodeinone terephthalate, 0.38 mg. homatropine terephthalate, 224 mg. acetylsalicylic acid, 160 mg. phenacetin, and 32 mg. caffeine.

*U.S. Pat. [illegible]

AND THE PAIN WENT AWAY FAST

Endo®

Literature? Write
ENDO LABORATORIES
Richmond Hill 18, New York

common denominator: a.p.

Worlds apart—plumber, pediatrician, press agent, counterman—these people have one thing in common: angina pectoris. Each one is receiving Peritrate 20 mg. q.i.d. as "basic therapy," providing long-acting coronary vasodilatation for fewer, less severe attacks, increased exercise tolerance, and reduced nitroglycerin dependence.

In one or another, however, underlying apprehensions, sudden stress situations, unpredictable daily schedules call for "basic therapy" **plus** individualized treatment. Broad coverage protection for each patient is afforded by a Peritrate formulation in terms of

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in
angina
aectoris

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brand of pentaerythritol tetranitrate

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"basic therapy"
Peritrate 20 mg.

for the apprehensive patient
Peritrate with Phenobarbital

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for convenient 24-hour protection
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the first
effervescent
bulk laxative

new

Effergel

EXCELLENT RESULTS—greater hydrophilic capacity without the feeling of fullness (gelling takes place in the intestine — not in the stomach). Low viscosity permits uniform distribution throughout intestinal contents.

PLEASANT TASTING—delightfully refreshing, lemon-flavored effervescent liquid assures patient cooperation.

FLEXIBLE—dosage can be varied according to the needs of adults, geriatrics, children, pre- and post-operative patients... everyone.

EASY-TO-TAKE—looks good. Really tastes good. Clear, attractive, effervescent drink.

CONTENTS:

Each 7 Gm. (approximately 1 rounded teaspoonful) provides:
Sodium Carboxymethylcellulose....2 Gm.
Di(acetylhydroxyphenyl)isatin .....6 mg.
(chemically similar to the active principle of prunes)
Supplied: 9 oz. bottles at all pharmacies.

DOSAGE:

Adults: initially, 1 rounded teaspoonful in a glass of water, morning and night. Dosage may be increased or decreased to suit needs.

Children 3 years and over: initially, 1 level teaspoonful in one-half glass of water upon retiring. Subsequent dosage to be adjusted according to results.

Stuart

THE STUART COMPANY • PASADENA, CALIFORNIA

when feathers stir up an allergic storm

Chlor-Trimeton Repetabs 8 or 12 mg.

(In Canada, CHLOR-TRIPOLON®)

Also available as 4 mg. tablets.

CHLOR-TRIMETON® Maleate, brand of Chlorprophenpyridamine Maleate U.S.P.
REPETABS,® Repeat Action Tablets.

SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY

SYMBOL OF THE ONE-DOSE CONVENIENCE YOU WANT FOR YOUR PATIENT.

• PROMPT REPETAB RELIEF • LASTS ALL DAY OR NIGHT •

Schering

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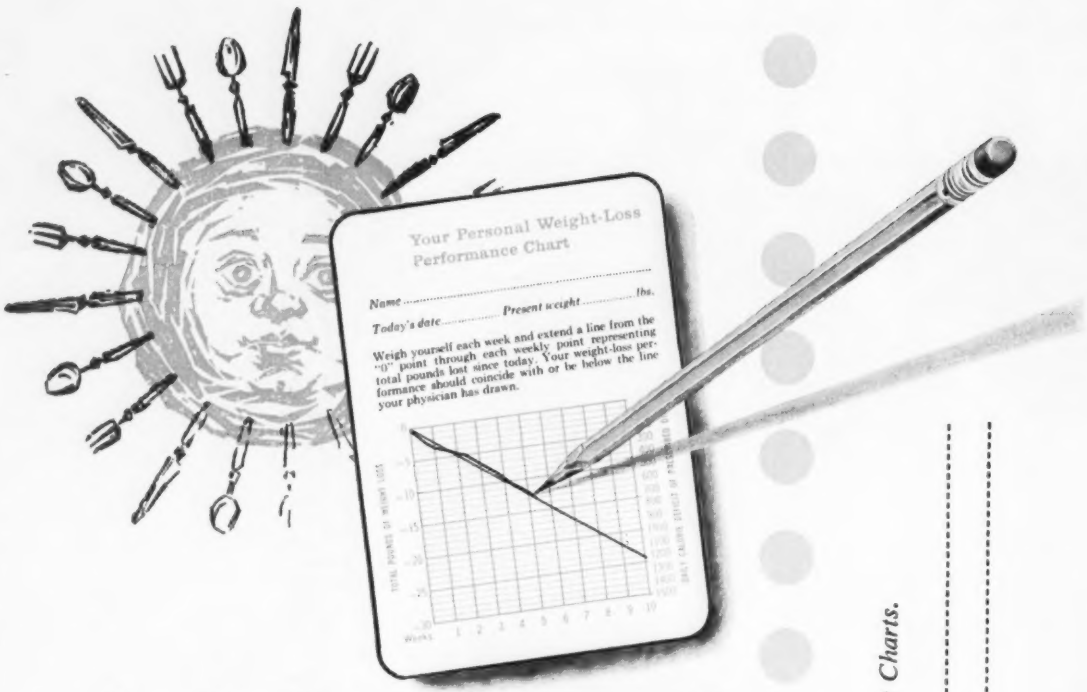
Your Personal Weight-Loss
Performance Chart
Name
Present weight
lbs.
Today's date
Weigh yourself each week and extend a line from the "0" point through each weekly point representing total pounds lost since today. Your weight-loss performance should coincide with or be below the line your physician has drawn.

in obesity management ...the incentive plan

YOUR PATIENT CHARTS HIS OWN PERFORMANCE LINE against your PREDICTION LINE

In giving each patient his ten-week chart of predicted weight-loss, you provide weekly goals as incentives for adhering strictly to your prescribed diet.

As the patient records his weight-loss performance week by week on the same chart, he experiences the satisfaction of achieving these goals you have set. And, equally important, he quickly sees the consequences of caloric overindulgence.

Each packet of ten charts includes a calorie nomogram —a time-saver in determining predicted weight-loss on the reducing diet you prescribe.

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in over three years of clinical use
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Specific

FOR RELIEF OF ANXIETY
AND MUSCLE TENSION

Selective

Does not interfere with autonomic function
Does not impair mental efficiency,
motor control, or normal behavior
Has not produced hypotension,
agranulocytosis or jaundice

MEPROBAMATE (WALLACE)

Miltown®

Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets.

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THE HEART DISEASE PATIENT NEEDS RELIEF FROM EMOTIONAL STRESS

ANXIETY INTENSIFIES the physical disorder in heart disease. "The prognosis depends largely on the ability of the physician to control the anxiety factor, as well as the somatic disease."

(Friedlander, H. S.: The role of ataraxics in cardiology. Am. J. Cardiol. 1:395, March 1958.)

TRANQUILIZATION WITH MILTOWN enhances recovery from acute cardiac episodes and makes patients more amenable to necessary limitations of activities.

(Waldman, S. and Pelner, L.: Management of anxiety associated with heart disease. Am. Pract. & Digest Treat. 8:1075, July 1957.)

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Available in 400 mg. scored and 200 mg. sugar-coated tablets. Also available as MEPROSPAN® (200 mg. meprobamate *continuous release* capsules). In combination with a nitrate, for angina pectoris: MILTRATE® (Miltown 200 mg. + PETN 10 mg.).

Miltown causes no adverse effects on heart rate, blood pressure, respiration or other autonomic functions.

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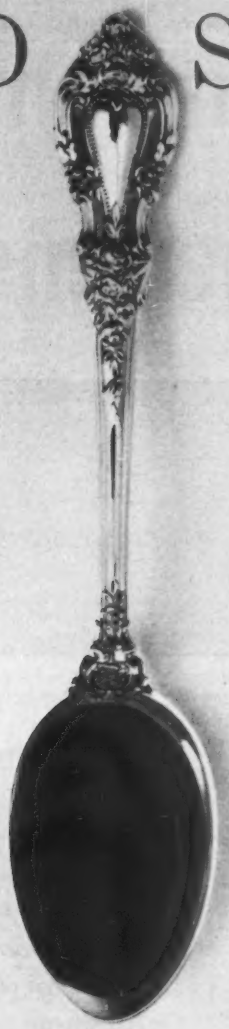
A SPOON LICKIN' GOOD SULFA!



it's delicious cherry-flavored for children

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ACETYL PEDIATRIC SUSPENSION

N¹ Acetyl Sulfamethoxypyridazine Lederle

just 1 dose a day... achieves rapid therapeutic levels... sustained for 24 hours... extremely low incidence of sensitivity reactions and renal complications... convenient, highly economical... ALWAYS ACCEPTABLE... WHENEVER SULFAS ARE INDICATED

Recommended dosage: first-day dose is 1 teaspoonful (250 mg.) for each 20 lbs. body weight up to 80 lbs. For each day thereafter, ½ teaspoonful for each 20 lbs. For 80 lbs. and over, use adult dosage of 4 teaspoonfuls (1.0 Gm.) initially, and 2 teaspoonfuls (0.5 Gm.) daily thereafter. Administer immediately after a meal.

Supplied: Each teaspoonful (5 cc.) contains 250 mg. of sulfamethoxypyridazine activity. Bottles of 4 and 16 fl. oz.

Lederle LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

Classic Treatment in Hypertension*

When more potent drugs are needed, prescribe one of the *convenient single-tablet combinations*

***Rauwiloid*® + *Veriloid*®**
alseroxylon 1 mg. and alkavervir 3 mg.
or
Rauwiloid*® + *Hexamethonium
alseroxylon 1 mg. and hexamethonium chloride dihydrate 250 mg.

Many patients with severe hypertension can be maintained on Rauwiloid alone after desired blood pressure levels are reached with combination medication.

* ***Because***

RAUWILOID provides effective Rauwolfia action virtually free from serious side effects ... the smooth therapeutic efficacy of Rauwiloid is associated with a lower incidence of certain unwanted side effects than is reserpine...and with a lower incidence of depression. Tolerance does not develop.

RAUWILOID can be initial therapy for most hypertensive patients...Dosage adjustment is rarely a problem.

Riker
Northridge, California

WASHINGTON NEWS

Opposition to Administration Health Insurance Plan . .
Accidental Poisoning Cases Surveyed . .
Government Seeks New Coloring Law . .
Hospitals Ask Federal Loans . .
President Directs Fall-Out Study . .
Miscellany . .

HEALTH GROUPS CHALLENGE ADMINISTRATION'S HEALTH INSURANCE PLAN

The administration's proposal for health and medical insurance for civilian government employes has encountered opposition at senate hearings.

Blue Cross, Blue Shield, and the American Hospital Association came out against the plan proposed by the Civil Service Commission, joining federal employee unions and other organized labor groups that also have criticized the administration's recommendations.

Similar disputes have blocked final congressional action in past years, even though all sides agree that government workers should be entitled to health and medical insurance coverage similar to that offered many workers in private industry.

The issue is being considered by a Senate Post Office and Civil Service subcommittee headed by Sen. Richard Neuberger (D., Ore.).

Witnesses representing Blue Cross, Blue Shield, and the Hospital Association in general supported legislation introduced by Sen. Olin Johnston (D., S. C.) but with reservations on some provisions.

The three organizations opposed deductibility features of the administration program and agreed that all medical services should be handled through a single source rather than allowing a different carrier to underwrite major medical expenses and another basic medical costs.

The administration asked that employees pay for the first $50 of hospitalization or medical costs. The three organizations argued that this would add to administrative expenses. Under the administration's proposal, private insurance companies could participate in the major medical or catastrophy plan. However, administration witnesses stressed the desirability of limiting the number of companies participating to as few as possible—"ideally, one."

The administration plan is somewhat more limited than the Johnston proposal. It places a $15,000 limit on major medical coverage, for example, while the Senator's measure sets no ceiling. And there are no deductibility provisions in the Johnston proposal. Blue Cross also recommended that a limitation be established.

ACCIDENTAL POISONING CASES ANALYZED

The only effective solution to the problem of children swallowing poisonous doses of substances is for the parents to keep them out of reach of youngsters and infants, according to Arthur S. Flemming, Secretary of Health, Education, and Welfare.

He made the statement in releasing an analysis of 4,000 accidental poisoning cases of all ages that was compiled by the National Clearing House for Poison Control Centers from reports from centers across the country.

Of the cases studied, one-fourth involved poisoning of infants eating large quantities of aspirin, "most of them small children who swallowed candied aspirin." Ninety per cent of the 4,000 cases involved children and were typical of the accidents that account for almost 500 children deaths and an estimated 600,000 nonfatal poisonings of children annually.

Food and Drug Commissioner George P. Larrick said that banning candied aspirin isn't the answer to aspirin or other poisoning incidents. "I don't believe you can solve the problem by eliminating pleasant-tasting medicines," he said. The official noted that candied aspirin must bear a label directing parents to keep it out of the reach of children.

Mr. Flemming said that "many serious consequences of poisoning could be prevented if parents called physicians promptly without waiting for symptoms to appear."

Among the products cited in the study as causing accidental poisoning were bleaches, detergents, waxes, polishes, cosmetics, insecticides, and lighter fluids, as well as all types of medicines and drugs.

The FDA doesn't have power to regulate labelling of products other than drugs and medicines. Mr. Larrick said the administration may decide soon whether to request such authority.

GOVERNMENT SEEKS NEW COLORING LAW

The administration is stepping up its campaign to ban or regulate harmful coloring substances in foods, drugs, and cosmetics.

Under a measure being sent to Congress, all colors would be regulated, not just coal-tar colors, and the Food and Drug Administration could set limits on the amounts used in products. Present law requires that if use of a color in quantity proves harmful to humans, the manufacturer must drop the color entirely from the product even though its use in small quantities is harmless.

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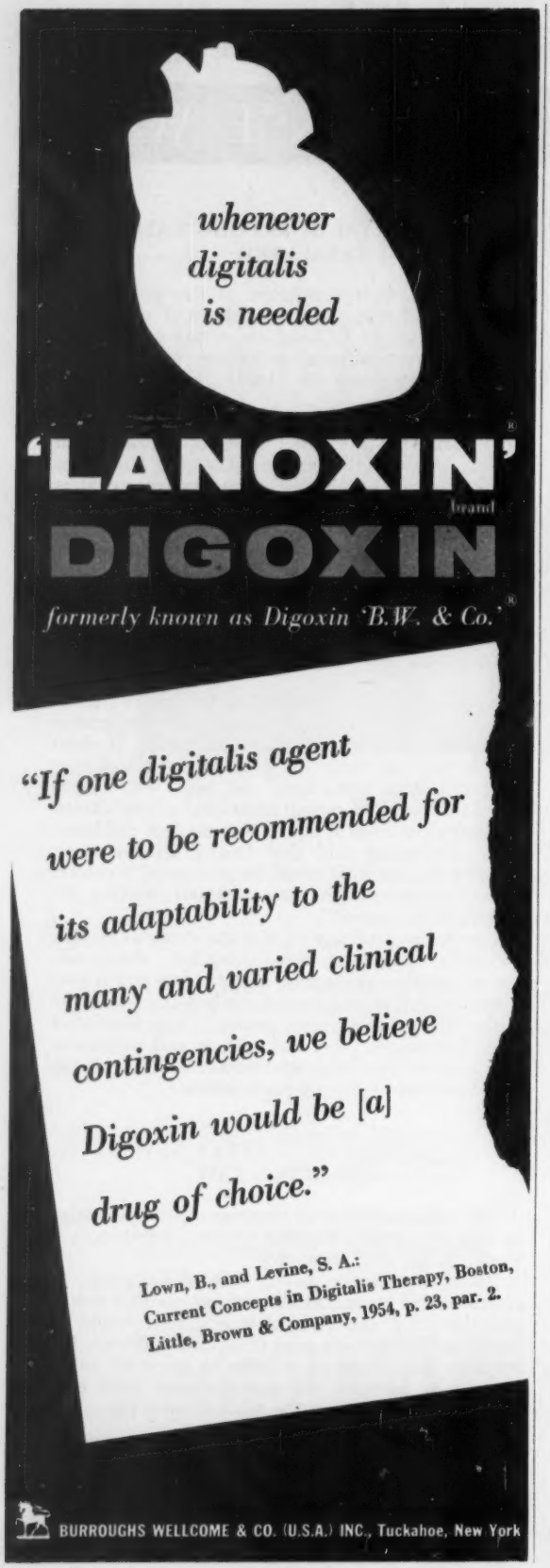
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is needed
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brand
DIGOXIN
formerly known as Digoxin 'B.W. & Co.'®
"If one digitalis agent were to be recommended for its adaptability to the many and varied clinical contingencies, we believe Digoxin would be [a] drug of choice."
Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.
BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

Companies would have to prove to the government's satisfaction that colors are safe, and the government would be allowed to test the products before they are marketed.

FDA has proposed closing of a loophole under which batches of a product ruled unsafe may continue to be sold because they had previously been certified safe. Products in warehouses destined for shipment or moving in interstate commerce at the time of a ruling would not be permitted to be sold.

In a related field, the agency, carrying out provisions of the new chemical additives act, published a list of 150 seasonings and flavorings generally considered to be safe for use in food. The list includes all of the most common household seasonings, such as paprika and vanilla, and such rare items as zedoary bark and pipsissewa leaves.

LOAN PROGRAM FOR HOSPITALS SOUGHT

A 500 million dollar revolving loan fund for construction of new hospitals and modernization of old ones was proposed to Congress by the American Hospital Association. The program would be part of a 1 billion dollar measure to provide low-interest long-term federal loans to communities for hospitals, parks, sewers, and other local public works.

According to an association spokesman in testimony on a community facilities bill before a House Banking subcommittee, a survey showed that 174,292 additional general hospital beds costing some 3.5 billion dollars are needed, plus more than 1 billion dollars for hospital modernization.

PRESIDENT ORDERS FALL-OUT PROBE

Three federal agencies have been directed by President Eisenhower to figure out the best way for the government to evaluate the effect of radioactive fall-out on health.

The Atomic Energy Commission, the Department of Health, Education, and Welfare, and the Budget Bureau are expected to release a report this month.

The study was ordered "in view of the considerable public attention which has been focused recently on the radiological health studies of the federal government," according to White House press secretary James C. Hagerty.

The three-agency study is not itself an investigation of the health effects of fall-out but rather an effort to determine the role of different federal agencies in the field.

A Senate-House atomic energy subcommittee will hold hearings on the matter starting May 4. Some committee members have expressed concern over some reports of a sharp increase in soil radioactivity and have proposed that the Public Health Service assume major responsibility in the field.

Atomic Energy Commissioner Willard F. Libby has said that his agency hopes to come up with significant findings on fall-out in time for the Congressional sessions. Dr. Libby reported recently that last fall's nuclear tests by the Soviet Union in the Arctic were followed by the sharpest rise yet in the radioactive contents of the stratosphere.

MISCELLANY

About one-third of the approximately 7,000 new physicians each year in the U. S. receive training in Veterans Administration hospitals, according to VA

Administrator Sumner G. Whittier. He said such training is conducted primarily to raise the quality of care furnished veteran-patients, and to help recruit scarce category personnel for the VA hospital staffs.

The Association of Food and Drug Officials says a survey of display cabinets in 3,063 stores in 34 states showed that nearly half the cabinets tested showed product temperatures above the recommended reading of 0 F.

Deputy Commissioner John L. Harvey of the Food and Drug Administration warns of new pesticides so potent that no residue is permissible on foods. He says the introduction of such pesticides with synthetic organic chemicals has created a pressing need for simpler and faster methods of detecting and identifying residues on foods.

The Food and Drug Administration moved to make it easier for persons on sugar-restricted diets to pick out artificially sweetened canned fruits. Under proposed new standards, the words "artificially sweetened" will appear on the label ahead of the name of the fruit. The labeling applies to artificially sweetened peaches, apricots, pears, cherries, fruit cocktail, and figs.

The Department of Health, Education, and Welfare for the first time has ordered a municipality to develop a water pollution control program.

Sioux City, Iowa, and 10 meat processing plants were directed to halt discharging untreated wastes into the Missouri River under the enforcement provisions of the 1956 Federal Water Pollution Control Act. The waste matter, a federal hearing board concluded, "constitutes a continuous danger of introduction of disease organisms."

The Public Health Service has reported that tuberculosis, once the leading cause of death among Indians and Alaska natives, dropped 40% among Indians in the four-year period ending in 1957. The decrease was 65% among Alaskan natives.

In addition, the Indian infant death rate has been reduced 12%, according to PHS. HEW Secretary Arthur S. Flemming commented that the PHS efforts with the Indians is "one of the nation's most dramatic health stories of our time."

The Defense Department compiled a special memorandum for physicians who are members of the stand-by reserve to bring specifically to their attention significant and applicable defense policies regarding inactive medical department reservists. The memo was intended for complete publication in the *Navy Medical News Letter*, Bureau of Medicine and Surgery *News*, the *Naval Reservist*, the *Navy Times*, and the *New Physician*.

HEW Secretary Flemming called for incorporating protection against mental illness in voluntary health insurance plans. This, he said, "would go a long way toward encouraging people with incipient mental or emotional disorders to obtain professional advice and assistance before their ailments reached a serious stage." Representative of National Committee against Mental Illness, Inc., testified along this line before Senate Civil Service Subcommittee during hearings on federal employee health insurance hearings.

The Food and Drug Administration assured the public that the great bulk of fish is not treated with nitrites or any other preservatives that might cause injury. Noting the death of a child in New Jersey from eating fish that had been treated with large quantities of sodium nitrite, the agency said any use of nitrites in fish is illegal.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice President.
1959 Annual Meeting, Atlantic City, June 8-12.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.

AMERICAN

1959

May

AMERICAN ASSOCIATION FOR THE HISTORY OF MEDICINE, Wade Park Manor, Cleveland, May 21-23. Dr. John B. Blake, Smithsonian Institution, Washington 25, D. C., Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Hotel Schroeder, Milwaukee, May 19-23. Dr. Neil A. Dayton, Mansfield State Training School & Hospital, Mansfield Depot, Conn., Secretary-Treasurer.

AMERICAN COLLEGE OF CARDIOLOGY, Benjamin Franklin Hotel, Philadelphia, May 26-29. Dr. Philip Reichert, 480 Park Ave., New York 22, Secretary.

AMERICAN COLLEGE HEALTH ASSOCIATION, Warwick Hotel, Philadelphia, May 6-9. Dr. Bruce S. Roxby, Temple University Health Service, Broad St. & Montgomery Ave., Philadelphia 22, Chairman, Committee on Local Arrangements.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Chalfonte-Haddon Hall, Atlantic City, N. J., May 3. Dr. George E. Schreiner, Georgetown Univ. Hosp., Washington 7, D. C., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 21-23. Dr. Andrew A. Marchetti, 3800 Reservoir Rd., N. W., Washington 7, D. C., Secretary.

AMERICAN OPHTHALMOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 28-30. Dr. Maynard C. Wheeler, 30 West 59th St., New York 19, Secretary.

AMERICAN PEDIATRIC SOCIETY, The Inn, Buck Hill Falls, Pa., May 6-8. Dr. A. C. McGuinness, 2800 Quebec St., Washington 8, D. C., Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Chalfonte-Haddon Hall, Atlantic City, N. J., May 2-3. Dr. Morton F. Reiser, 265 Nassau Rd., Roosevelt, N. Y., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Haddon Hall, Atlantic City, N. J., May 3-4. Dr. S. J. Farber, 550 1st Ave., New York 16, Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Palmer House, Chicago, May 10-14. Dr. Orion H. Stuteville, 700 N. Michigan, Chicago 11, Secretary.

AMERICAN TRUDEAU SOCIETY, Palmer House, Chicago, May 25-27. Dr. E. P. K. Fenger, 1790 Broadway, New York 19, Secretary.

AMERICAN UROLOGICAL ASSOCIATION, WESTERN SECTION, Monterey, Calif., May 17-21. Dr. James Ownby Jr., 516 Sutter St., San Francisco, Registration Chairman.

ASSOCIATION OF AMERICAN PHYSICIANS, Haddon Hall, Atlantic City, N. J., May 5-6. Dr. Paul B. Beeson, Yale Univ. School of Medicine, New Haven 11, Conn., Secretary.

ASSOCIATION OF SURGEONS OF THE SOUTHERN RAILWAY SYSTEM, Netherland Hilton Hotel, Cincinnati, May 4-5. Dr. J. Marsh Frere, 705-9 Walnut St., Chattanooga 2, Tenn., Secretary.

FLORIDA MEDICAL ASSOCIATION, Americana Hotel, Miami Beach, May 2-6. Mr. Ernest R. Gibson, P. O. Box 2411, Jacksonville 3, Managing Director.

GEORGIA, MEDICAL ASSOCIATION OF, Bon Air Hotel, Augusta, May 17-20. Mr. Milton D. Kreuger, 875 W. Peachtree St., N. W., Atlanta, Executive Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 19-22. Dr. Harold M. Camp, 224 S. Main St., Monmouth, Secretary.

INTERNATIONAL COLLEGE OF SURGEONS, ALABAMA SURGICAL SECTION, Erskine Hotel, Huntsville, May 21-22. Dr. E. V. Caldwell, 2515 Memorial Pkwy., S. E., Huntsville, Ala., General Chairman.

INTERNATIONAL COLLEGE OF SURGEONS, NEW YORK STATE SECTION, Concord Hotel, Kiamesha Lake, May 28-31. Dr. Milton S. Weinberg, 3741 75th St., Jackson Heights, N. Y., Chairman, Arrangements Committee.

KANSAS MEDICAL SOCIETY, Jayhawk Hotel, Topeka, May 3-7. Mr. Oliver E. Ebel, 315 W. 4th St., Topeka, Executive Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Roosevelt Hotel, New Orleans, May 4-6. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Executive Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 19-21. Dr. Robert W. Buck, 22 The Fenway, Boston 15, Secretary.

MINNESOTA STATE MEDICAL ASSOCIATION, Hotel Duluth, Duluth, May 25-27. Mr. R. R. Rosell, 496 Lowry Medical Arts Bldg., St. Paul 2, Minn., Executive Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Hotel Buena Vista, Biloxi, May 12-14. Mr. Rowland B. Kennedy, 735 Riverside Dr., Jackson, Executive Secretary.

NATIONAL CONFERENCE ON WORLD HEALTH (SECOND), Statler Hotel, Washington, D. C., May 7-9. Mr. Philip E. Nelbach, National Citizens Committee for WHO, 1790 Broadway, New York 19, Executive Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Palmer House, Chicago, May 24-29. Mrs. Wallace B. White, 1790 Broadway, New York 19, Secretary.

NEVADA ACADEMY OF GENERAL PRACTICE, Hotel Riverside, Reno, May 21-23. For information write Dr. Roy M. Peters, 495 S. Arlington Ave., Reno, Nev.

NEW MEXICO MEDICAL SOCIETY, Mission Mote, Las Cruces, May 5-7. Mr. Ralph R. Marshall, 221 W. Central Ave., Albuquerque, Executive Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, Buffalo, May 9-13. Dr. Walter P. Anderton, 386 Fourth Ave., New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, George Vanderbilt Hotel, Asheville, May 3-6. Mr. James T. Barnes, 203 Capitol Club Bldg., Raleigh, Executive Director.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Prince Hotel, Bismarck, May 2-5. Mr. Lyle A. Limond, Box 1198, Bismarck, Executive Secretary.

NORTHERN TRI-STATE POST-GRADUATE MEDICAL ASSOCIATION, Schuler Hotel, Marshall, Mich., May 7. Dr. Francis E. Elliott, 130 N. Fulton St., Wauseon, Ohio, Secretary-Treasurer.

OGDEN SURGICAL SOCIETY, Ogden, Utah, May 20-22. Dr. O. E. Grua, 412 First Security Bldg., Ogden, Utah, Secretary.

OHIO VALLEY PROCTOLOGIC SOCIETY, French Lick, Ind., May 14. Dr. Gerson Carmel, 214 Doctors Bldg., Cincinnati 2, Secretary.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY, Hotel Riviera, Las Vegas, Nev., May 3-7. Dr. Homer E. Smith, 686 Twelfth Ave., Salt Lake City 3, Utah, Executive Secretary-Treasurer.

RHODE ISLAND MEDICAL SOCIETY, Providence, May 12-13. Mr. John E. Farrell, 106 Francis St., Providence 3, Executive Secretary.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Sheraton Jefferson Hotel, St. Louis, May 10-15. Dr. E. M. Foster, University of Wisconsin, Madison 6, Wis., Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, The Inn, Buck Hill Falls, Pa., May 8-9. Dr. Clark D. West, Children's Hosp., Cincinnati 29, Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Columbia Hotel, Columbia, May 12-14. Mr. M. L. Meadors, 309 W. Evans St., Florence, Executive Secretary.

SYMPOSIUM ON METAL-BINDING IN MEDICINE, Hahnemann Medical College, Philadelphia, May 6-8. For information write Dr. Marvin J. Seven, Hahnemann Medical College, 230 N. Broad St., Philadelphia 2.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder, Milwaukee, May 5-7. Mr. Charles H. Crownhart, P. O. Box 1109, Madison 1, Secretary.

June

AMERICAN ACADEMY OF TUBERCULOSIS PHYSICIANS, Atlantic City, N. J., June 6. Dr. Oscar S. Levin, P. O. Box 7011, Denver 6, Secretary.

AMERICAN COLLEGE OF ANGIOLOGY, WORLD CONFERENCE ON ANGIOLOGY, Marlborough Blenheim Hotel, Atlantic City, N. J., June 5-7. Dr. Alfred Halpern, 11 Hampton Court, Great Neck, N. Y., Executive Secretary.

AMERICAN COLLEGE OF CHEST PHYSICIANS, Atlantic City, N. J., June 3-7. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

AMERICAN DERMATOLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., June 1-4. Dr. Wiley M. Sams, 25 Southeast 2d Ave., Miami, Fla., Secretary.

AMERICAN DIABETES ASSOCIATION, Chalfonte-Haddon Hall, Atlantic City, N. J., June 6-7. Dr. E. Paul Sheridan, 1 East 45th St., New York 17, Secretary.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, Claridge Hotel, Atlantic City, N. J., June 11-14. Dr. Jerome K. Merlis, University Hospital, Baltimore 1, Secretary.

AMERICAN GASTROENTEROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., June 5-6. Dr. Franz J. Ingelfinger, 69 E. Newton St., Boston 18, Secretary.

AMERICAN GASTROSCOPIC SOCIETY, Atlantic City, June 7. Dr. Arthur M. Olsen, 200 First St., S. W., Rochester, Minn., Secretary-Treasurer.

AMERICAN GERIATRICS SOCIETY, Hotel Traymore, Atlantic City, N. J., June 4-5. Dr. Richard J. Kraemer, 2907 Post Rd., Warwick, R. I., Secretary.

AMERICAN MEDICAL ASSOCIATION, Traymore Hotel, Atlantic City, N. J., June 8-12. Dr. F. J. L. Blasingame, 535 N. Dearborn St., Chicago 10, Executive Vice-President.

AMERICAN MEDICAL WOMEN'S ASSOCIATION, Sheraton Ritz Carlton Hotel, Atlantic City, N. J., June 4-7. Miss Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN NEUROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., June 15-17. Dr. Charles Rupp, 133 S. 36th St., Philadelphia 4, Secretary.

AMERICAN ORTHOPEDIC ASSOCIATION, Lake Placid Club, Lake Placid, N. Y., June 16-18. Dr. Lee Ramsey Straub, 535 E. 70th St., New York 21, Secretary.

AMERICAN PHYSICAL THERAPY ASSOCIATION, Hotel Leamington, Minneapolis, June 21-26. Miss Annetta Cornell Wood, 1790 Broadway, New York 19, Executive Director.

AMERICAN PROCTOLOGIC SOCIETY, Shelburne Hotel, Atlantic City, N. J., June 15-18. Dr. Norman D. Nigro, 10 Peterboro St., Detroit 1, Secretary.

AMERICAN RHEUMATISM ASSOCIATION, Mayflower Hotel, Washington, D. C., June 2-6. Dr. Edward F. Hartung, 580 Park Ave., New York 21, Secretary.

AMERICAN THERAPEUTIC SOCIETY, Shelburne Hotel, Atlantic City, N. J., June 4-7. Dr. Oscar B. Hunter Jr., 915-19th St., N. W., Washington 6, D. C., Secretary.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC., Atlantic City, N. J., June 8-12. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

CATHOLIC HOSPITAL ASSOCIATION OF THE UNITED STATES AND CANADA, St. Louis, June 1-4. Mr. M. R. Kneiff, 1438 S. Grand Blvd., St. Louis 4, Executive Secretary.

GASTROENTEROLOGY RESEARCH GROUP, Claridge Hotel, Atlantic City, N. J., June 4. For information write Dr. Charles F. Code, Mayo Clinic, Rochester, Minn.

IDAHO STATE MEDICAL ASSOCIATION, Sun Valley, June 14-17. Mr. Armand L. Bird, 364 Sonna Bldg., Boise, Executive Secretary.

INTERMOUNTAIN PEDIATRIC SOCIETY, Sun Valley, Idaho, June 26-28. Dr. J. R. Newton, Memorial Medical Center, 2000 S. 9th E., Salt Lake City, Utah, Publicity Chairman.

(Continued on page 32)

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1. Farquharson, R. F.: The menopausal patient. M. Rec. & Ann. 49:196, Feb. 1955.

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INTERNATIONAL CARDIOVASCULAR SOCIETY, NORTH AMERICAN CHAPTER, Hotel Shelburne, Atlantic City, N. J., June 6. Dr. Paul T. DeCamp, 3503 Prytania St., New Orleans, Secretary.

MAINE MEDICAL ASSOCIATION, The Samoset, Rockland, June 21-23. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Executive Director.

MEDICAL LIBRARY ASSOCIATION, King Edward-Sheraton Hotel, Toronto, Can., June 15-19. Miss Nettie A. Mehne, The Upjohn Co., Kalamazoo, Mich., Secretary.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY, Ritz Carlton Sheraton Hotel, Atlantic City, N. J., June 6-7. Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Claridge Hotel, Atlantic City, N. J., June 13-14. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Secretary.

SOCIETY OF NUCLEAR MEDICINE, Palmer House, Chicago, June 18-20. Dr. Morris T. Friedell, 104 S. Michigan Ave., Chicago 3, Chairman, Press & Public Relations Committee.

SOUTH DAKOTA STATE MEDICAL ASSOCIATION, Sheraton Johnson Hotel, Rapid City, June 20-23. Mr. John C. Foster, 300, 1st National Bank Bldg., Sioux Falls, Executive Secretary.

THE ENDOCRINE SOCIETY, Chalfonte-Haddon Hall, Atlantic City, N. J., June 4-6. Dr. Henry T. Turner, 1200 N. Walker St., Oklahoma City 3, Secretary.

WYOMING STATE MEDICAL ASSOCIATION, Jackson Lake Lodge, Moran, June 11-14. Mr. Arthur R. Abbey, Box 2036, Cheyenne, Executive Secretary.

July

AMERICAN SOCIETY OF FACIAL PLASTIC SURGERY, New York City, July 17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

AMERICAN SOCIETY OF X-RAY TECHNICIANS, Shirley Savoy Hotel, Denver, July 4-9. Miss Genevieve J. Eilert, 16 14th St., Fond du Lac, Wis., Executive Secretary.

OREGON CANCER CONFERENCE, University of Oregon Medical School, Portland, July 16-17. Dr. Martin A. Howard, 1115 S. W. Taylor St., Portland 5, Ore., Chairman.

ROCKY MOUNTAIN CANCER CONFERENCE, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

AMERICAN CONGRESS OF PHYSICAL MEDICINE AND REHABILITATION, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

AMERICAN DIETETIC ASSOCIATION, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

AMERICAN HOSPITAL ASSOCIATION, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

AMERICAN VETERINARY MEDICAL ASSOCIATION, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION, INC., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

NATIONAL MEDICAL ASSOCIATION, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

NEVADA STATE MEDICAL ASSOCIATION, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

AMERICAN ASSOCIATION OF MEDICAL CLINICS, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

AMERICAN ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts, Jr., 3400 Spruce St., Philadelphia 4, Secretary.

AMERICAN COLLEGE OF GASTROENTEROLOGY, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

AMERICAN COLLEGE OF SURGEONS, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

AMERICAN COLLEGE OF SURGEONS, OHIO CHAPTER, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

AMERICAN ROENTGEN RAY SOCIETY, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

AMERICAN SOCIETY OF CLINICAL PATHOLOGISTS, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

COLLEGE OF AMERICAN PATHOLOGISTS, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

COLORADO STATE MEDICAL SOCIETY, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

KENTUCKY STATE MEDICAL ASSOCIATION, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

MEDICAL PROGRESS ASSEMBLY, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

MICHIGAN STATE MEDICAL SOCIETY, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

MID-CONTINENT PSYCHIATRIC ASSOCIATION, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

MONTANA MEDICAL ASSOCIATION, Finlen Hotel, Butte, Sept. 17-19. Mr. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executive Secretary.

NORTH AMERICAN FEDERATION, INTERNATIONAL COLLEGE OF SURGEONS, Chicago, Sept. 13-17. For information write the Secretariat, 1516 Lake Shore Dr., Chicago 10.

OREGON STATE MEDICAL SOCIETY, Medford Hotel, Medford, Sept. 23-25. Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executive Secretary.

UNITED STATES SECTION, INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Shore Dr., Chicago 10, Executive Secretary.

UTAH STATE MEDICAL ASSOCIATION, Hotel Utah Motor Lodge, Salt Lake City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City 2, Executive Secretary.

WASHINGTON STATE MEDICAL ASSOCIATION, Olympic Hotel, Seattle, Sept. 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

WORLD MEDICAL ASSOCIATION, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

ACADEMY OF PSYCHOSOMATIC MEDICINE, Sheraton-Cleveland Hotel, Cleveland, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Secretary.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, The Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Executive Secretary.

AMERICAN ACADEMY OF PEDIATRICS, The Palmer House, Chicago, Oct. 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

AMERICAN ASSOCIATION OF MEDICAL RECORD LIBRARIANS, Radisson Hotel, Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St., Chicago 10, Director.

AMERICAN COLLEGE OF CHEST PHYSICIANS, 25th Anniversary Homecoming Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

AMERICAN COLLEGE OF PREVENTIVE MEDICINE, Hotel Ambassador, Atlantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C., Secretary-Treasurer.

AMERICAN HEART ASSOCIATION, Trade and Convention Center, Philadelphia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New York 10, Secretary.

AMERICAN MEDICAL WRITERS' ASSOCIATION, St. Louis, Oct. 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

AMERICAN OTORHINOLOGIC SOCIETY FOR PLASTIC SURGERY, INC., Conrad Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., Detroit 24, Co-Chairman, Planning Committee.

AMERICAN PUBLIC HEALTH ASSOCIATION, Convention Hall, Atlantic City, N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, N. Y., Executive Director.

AMERICAN SCHOOL HEALTH ASSOCIATION, Claridge Hotel, Atlantic City, N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Executive Secretary.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS, INC., Americana Hotel, Bal Harbor, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St., Room 1101, Chicago 1, Executive Secretary.

AMERICAN SOCIETY OF FACIAL PLASTIC SURGERY, Chicago, Oct. 15-17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

AMERICAN SOCIETY OF PLASTIC AND RECONSTRUCTIVE SURGERY, Hotel Fountainebleau, Miami Beach., Fla., Oct. 18-23. Dr. Thomas Ray Broadbent, 508 E. South Temple, Salt Lake City, General Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Claypool Hotel, Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road, Miami 33, Fla., Executive Secretary.

ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS OF AMERICA, Hotel Statler Hilton, New York City, Oct. 21-23. Dr. Royal S. Schaaf, Prudential Insurance Co., P. O. Box 594, Newark 1, N. J., Secretary.

ASSOCIATION OF MEDICAL ILLUSTRATORS, Seattle, Oct. 5-7. Miss Rose M. Reynolds, University of Nebraska College of Medicine, 42nd Dewey Ave., Omaha 5, Corresponding Secretary.

CENTRAL NEUROPSYCHIATRIC ASSOCIATION, Hotel Roosevelt, New Orleans, Oct. 16-17. Dr. Ralph M. Patterson, Columbus Psychiatric Institute, 473 W. 12th Ave., Columbus 10, Ohio.

CONGRESS OF NEUROLOGICAL SURGEONS, Americana Hotel, Miami, Fla., Oct. 28-31. Dr. Richard L. DeSaussure, Suite 101 B, 20 S. Dudley St., Memphis, Tenn., Secretary-Treasurer.

DELAWARE, MEDICAL SOCIETY OF, Oct. 14-15. Mr. Lawrence J. Morris Jr., 621 Delaware Ave., Wilmington 1, Del.

(Continued on next page)

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INDIANA STATE MEDICAL ASSOCIATION, Murat Temple, Indianapolis, Oct. 6-9. Mr. James A. Waggener, 1021 Hume Mansur Bldg., Indianapolis 4, Executive Secretary.

NEW HAMPSHIRE MEDICAL SOCIETY, Equinox House, Manchester, Vt., Oct. 1-4. Mr. Hamilton S. Putnam, 18 School St., Concord, N. H., Executive Secretary.

PENNSYLVANIA, MEDICAL SOCIETY OF THE STATE OF, Penn-Sheraton Hotel, Pittsburgh, Oct. 18-23. Mr. Lester H. Perry, 230 State St., Harrisburg, Pa., Executive Director.

VERMONT STATE MEDICAL SOCIETY, Equinox House, Manchester, Oct. 1-4. Mr. Getty Page, 128 Merchants Row, Rutland, Vt., Executive Secretary.

VIRGINIA, MEDICAL SOCIETY OF, Hotel Roanoke, Roanoke, Oct. 4-5. Mr. Robert I. Howard, 4205 Dover Rd., Richmond 21, Va.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, INC., Statler Hotel, Los Angeles, Oct. 2-3. Dr. A. C. Remington, 9851 Sepulveda Blvd., Los Angeles 45, Secretary.

WESTERN ORTHOPEDIC ASSOCIATION, Brown Palace Hotel, Denver, Oct. 18-22. Vi Mathiesen, 354 21st St., Oakland 12, Calif., Executive Secretary.

November

AMERICAN ASSOCIATION OF BLOOD BANKS, Edgewater Beach Hotel, Chicago, Nov. 4-7. Dr. John B. Alsever, Southwest Blood Banks, 1211 W. Washington St., Phoenix, Ariz., Secretary.

AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, The Homestead, Hot Springs, Va., Nov. 2-4. Dr. F. Tremaint Billings, 420 Medical Arts Bldg., Nashville, Tenn., Secretary.

AMERICAN FRACTURE ASSOCIATION, Roosevelt Hotel, New Orleans, Nov. 1-3. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Executive Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, Edgewater Beach Hotel, Chicago, Nov. 2-4. Dr. Ward Darley, 2530 Ridge Ave., Evanston, Ill., Executive Director.

ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES, Mayflower Hotel, Washington, D. C., Nov. 8-11. Lt. Col. George M. Beam, AUS, Ret., Suite 718, New Medical Bldg., 1726 Eye St., N. W., Washington 6, D. C., Executive Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH, Drake Hotel, Chicago, Nov. 6-7. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Cleveland 6, Secretary.

CONFERENCE ON ELECTRICAL TECHNIQUES IN MEDICINE AND BIOLOGY, Sheraton Hotel, Philadelphia, Nov. 10-12. Dr. Herman P. Schwan, Moore School of Electrical Engineering, University of Pennsylvania, Philadelphia, Chairman.

DISTRICT OF COLUMBIA, MEDICAL SOCIETY OF, Statler-Hilton Hotel, Washington, D. C., Nov. Mr. Theodore Wiprud, 1718 M Street, N. W., Washington 6, D. C.

GASTROENTEROLOGY RESEARCH GROUP, Drake Hotel, Chicago, Nov. 6. For information write Dr. Charles F. Code, Mayo Clinic, Rochester, Minn.

GERONTOLOGICAL SOCIETY, INC., Statler Hotel, Detroit, Nov. 12-14. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Administrative Secretary.

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, The Palmer House, Chicago, Nov. 2-5. Mr. Roy T. Ragatz, Box 1109, Madison 1, Wis., Executive Secretary.

NATIONAL PROCTOLOGIC ASSOCIATION, Chicago, Nov. Dr. George E. Mueller, 59 E. Madison, Chicago 2, Secretary.

NATIONAL SOCIETY FOR CRIPPLED CHILDREN AND ADULTS, Palmer House, Chicago, Nov. 29-Dec. 2. Dr. Dean W. Roberts, 2023 W. Ogden Ave., Chicago 12, Executive Director.

OMAHA MID-WEST CLINICAL SOCIETY, Civic Auditorium, Omaha, Nov. 2-5. Mrs. Reta M. Crowell, 1031 Medical Arts Bldg., Omaha 2, Executive Secretary.

PUERTO RICO MEDICAL ASSOCIATION, Santurce, Nov. 22-26. Mr. J. A. Sanchez, Box 9111, Santurce 29, Puerto Rico, Executive Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, INC., Palmer House, Chicago, Nov. 15-20. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Secretary-Treasurer.

SOUTHERN MEDICAL ASSOCIATION, Atlanta, Nov. 16-19. Mr. V. O. Foster, 2601 Highland Ave., Birmingham 5, Ala., Executive Secretary-Treasurer.

WESTERN SURGICAL ASSOCIATION, The Broadmoor, Colorado Springs, Colo., Nov. 19-21. Dr. John T. Reynolds, 612 N. Michigan Ave., Chicago 11, Secretary.

December

NEW YORK HEART ASSOCIATION, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

1960

January

AMERICAN ACADEMY OF ALLERGY, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

February

AMERICAN ACADEMY OF OCCUPATIONAL MEDICINE, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

AMERICAN COLLEGE OF ALLERGISTS, INC., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

(Continued on page 36)

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American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Laryngological, Rhinological and Otological Society, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla., Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneapolis 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

California Medical Association, Hotel Ambassador, Los Angeles, Mar. 13-16. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

National Health Council, National Health Forum, Miami, Fla., Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Executive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. Mr. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 30-Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore 1, Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Mar. 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Executive Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev., Mar. 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma City, Okla., Executive Secretary.

April

American Association of Anatomists, Statler-Hilton, New York City, Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medicine, Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Railway Surgeons, Drake Hotel, Chicago, Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Executive Secretary.

American College of Obstetricians and Gynecologists, Netherland Hilton Hotel, Cincinnati, Apr. 3-6. Mr. Donald F. Richardson, P. O. Box 749, Chicago 90, Executive Secretary.

American Gastroenterological Association, Roosevelt Hotel, New Orleans, April 1-2. Dr. Franz J. Ingelfinger, 65 E. Newton St., Boston 18, Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Daggs, D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Secretary.

American Society for the Study of Sterility, Sheraton-Gibson Hotel, Cincinnati, Apr. 1-3. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham 5, Ala., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, The Alcazar, Baltimore, Apr. 20-22. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Tennessee State Medical Association, The Maxwell House, Nashville, Apr. 10-13. Mr. Jack E. Ballentine, 112 Louise Ave., Nashville 5, Tenn., Executive Director.

INTERNATIONAL AND FOREIGN

1959

May

Conference on International Union for Health Education of the Public, Dusseldorf, Germany, May 2-9. For information address: Secretary-General, 92, rue St. Denis, Paris 1, France.

Congress of the International Association for the Study of Bronchi, Madrid, May 29-30. Prof. Jose Abello, Lagasca 13, Madrid, Spain, Secretary-General.

International Congress of Acupuncture, Paris, France, May 9-11. For information address: 8 avenue Franklin Roosevelt, Paris 8e, France.

International Congress of Infectious Pathology (Second), Milan, Italy, May 6-10. Prof. Carlo Zanussi, Via Francesco Sforza, 35-(Istituto di Igiene dell'Università)-Milano, Italy, General Secretary.

International Congress on Irradiation of Endocrine Organs, Amsterdam, May 30-June 1. For information, write: Dr. Johanna M. van Went, Banstraat 30 hoek de Lairessestraat, Amsterdam Z I, Nederland.

International Hospital Equipment & Medical Service Exhibition (Second), Empire Hall, London, May 25-30. Mr. W. R. Kern, 40 Gerrard St., Piccadilly, London, W. 1, England, Organizer and Director.

International Symposium on the Prevention of Bacterial Resistance to Antibiotics, Perugia, Italy, May 1-3. For information write: Segreteria del Simposio, Clinica Ostetrica e Ginecologica, Policlinico, Perugia, Italy.

International Veterinary Congress, Madrid, Spain, May 21-27. Dr. Jac Jensen, Beistraat 168, Utrecht, Netherlands, General Secretary.

Middle East Medical Assembly, American University of Beirut, Lebanon, May 8-10. Dr. Calvin H. Plimpton, American University of Beirut, Beirut, Lebanon, Chairman.

World Health Assembly, Geneva, May 12 (three weeks). For information write: World Health Organization, Palais des Nations, Geneva, Switzerland.

June

Canadian Association of Physical Medicine and Rehabilitation (7th Annual Meeting), Lord Nelson Hotel, Halifax, N. S., June 4-6. Dr. M. Mongeau, 6265 Hudson Rd., Montreal 26, Que., Secretary.

Canadian Federation of Biological Societies (Canadian Physiological Society, Pharmacological Society of Canada, Canadian Association of Anatomists, Canadian Biochemical Society), University of Toronto, Toronto, Ont., Canada, June 9-11. Dr. E. H. Bensley, Room 710, The Montreal General Hospital, Montreal 25, Que.

Canadian Public Health Association (Jubilee Meeting), Sheraton Mount Royal Hotel, Montreal, Que., June 1-3, Dr. G. W. O. Moss, 150 College St., Toronto 5, Ont., Honorary Secretary.

Congress and International Exhibit of Technicians of Health, Parc des Expositions, Porte de Versailles, Paris, France, June 9-12. For information write the Secretariat of the Congress, 37, rue de Montholon, Paris 9e, France.

International Conference on Medical Electronics, UNESCO Bldg., Paris, June 24-27. Dr. F. Brackett, National Institutes of Health, Bethesda 14, Md., Regional Program Representative.

International Fertility Association, Amsterdam, Netherlands, June 7-13. For information address: Dr. B. S. ten Berge, Women's Hospital, Groningen, Netherlands.

International Hospital Congress, Edinburgh, Scotland, June 1-6. Capt. J. E. Stone, 34 King St., London, E. C. 2, England, Secretary-General.

Irish Medical Association, Killarney, June 29-July 3. Dr. Noel Reilly, 10, Fitzwilliam Place, Dublin, Ireland, Medical Secretary.

Pan-American Congress on Rheumatic Diseases, Washington, D. C., U. S. A., June 2-6. Dr. Richard T. Smith, West Point, Pa., U. S. A., Secretary-General.

July

British Medical Association, Edinburgh, Scotland, July 18-24. For information address: The Secretary, British Medical Association, Tavistock Square, London, W. C. 1, England.

Canadian Medical Association, Edinburgh, Scotland, July 18-24. Dr. A. D. Kelly, 150 St. George St., Toronto 5, Ont., General Secretary.

International Congress of Pediatrics, Montreal, Que., July 19-25. For information address: Dr. R. L. Denton, 2300 Tupper St., Montreal 25, Que.

International Congress of Plastic Surgery, London, England, July 13-17. Mr. David Matthews, 152 Harley St., London, W. 1, England.

International Congress of Radiology, Munich, Germany, July 23-30. Prof. Hans v. Braunbehrens, Frankfurt am Main, Forsthausstrasse 76, Germany, General Secretary.

International Congress of School and University Health (Third), Paris, France, July 6-8. For information write: Comite d'Organisation du Congres d'Hygiene Scolaire et Universitaire, 13, rue du Four, Paris 6e, France.

International Medical Conference on Mental Retardation (First), Eastland Hotel, Portland, Maine, July 27-31. Dr. Ella Langer, State House, Augusta, Me., Chairman, Committee on Finance and Arrangements.

International Psychoanalytical Association, Copenhagen, Denmark, July 26-30. Miss Pearl King, 37 Albion St., London, W. 2, England, Secretary-General.

International Union of the Medical Press (4th Congress), Cologne, Germany, July 3-5. Dr. Stockhausen, Brabanterstr. 13, Cologne, Germany, Secretary-General.

Shaio Foundation Symposium on Cardiovascular Diseases, Hotel Tequendama, Bogota, Colombia, July 27-31. Dr. Alberto Vejarano, Fundacion A. Shaio, Clinica: Carretera de Suba, Bogota, Colombia.

August

International Association of Limnology, Vienna & Salzburg, Austria, Aug. 20-Sept. 8. For information address: Secretary, Biologische Station, Lunz am See, Austria.

International Congress for the History of Science, Barcelona & Madrid, Spain, Aug. 30-Sept. 6. Prof. J. Vernet, Universidad de Barcelona, Barcelona, Spain, Secretary-General.

International Congress of Physiological Sciences, Buenos Aires, Argentina, Aug. 9-15. A. O. M. Stoppani, Facultad de Ciencias Medicas, Paraguay 2151, Buenos Aires, Argentina.

International Congress for Speech and Voice Therapy, London, England, Aug. 17-22. Miss M. Carter, 46 Cannonbury Square, London, N. 1, England, Secretary.

Pan-American Congress of Veterinary Medicine, Kansas City, Mo., U. S. A., Aug. 23. Dr. Benjamin D. Blood, P. O. Box 99, Azul, Buenos Aires Province, Argentina, Secretary-General.

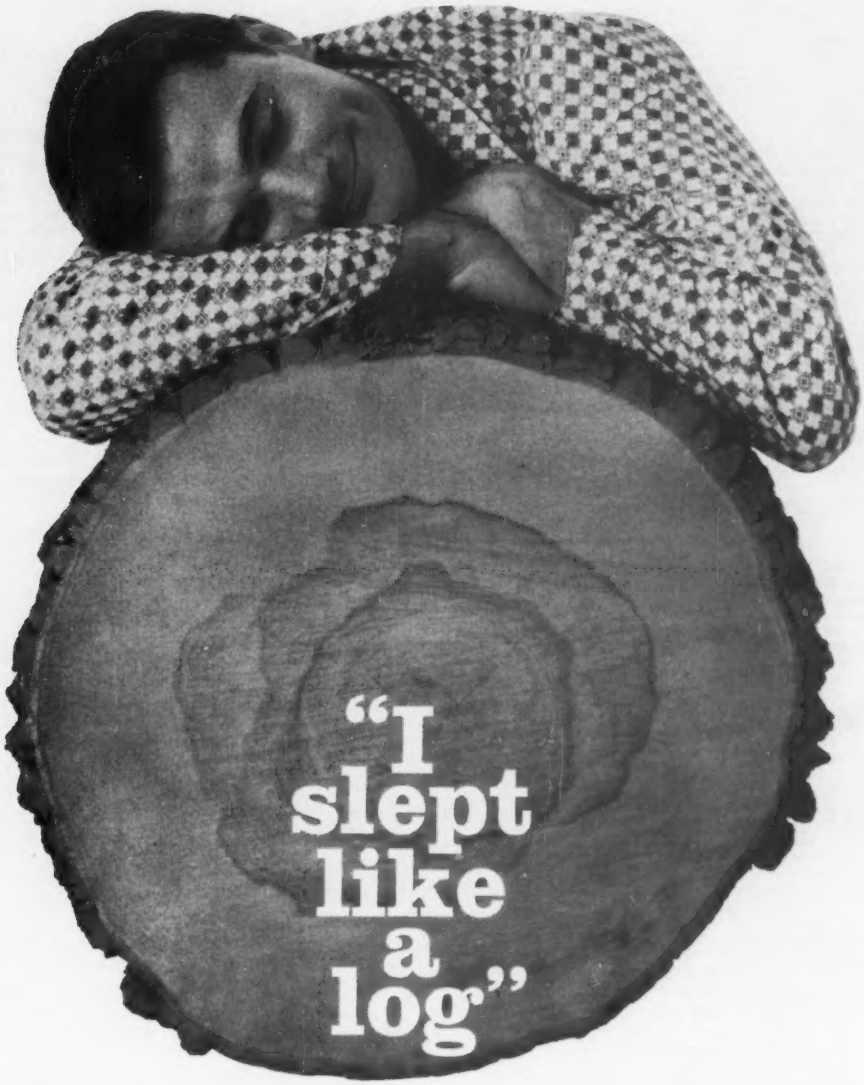
World Conference on Medical Education, Palmer House, Chicago, Ill., U. S. A., Aug. 30-Sept. 4. For information address: Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, N. Y., U. S. A.

World Federation for Mental Health, Barcelona, Spain, Aug. 30-Sept. 5. Miss Esther M. Thornton, 19 Manchester St., London, W. 1, England, Secretary-General.

September

Congress of International Union of Railway Medical Services, Lucerne, Switzerland, Sept. 21-24. Dr. J. Ortega, 13, rue de Chateau-London, Paris 10, France, Secretary-General.

(Continued on page 38)



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European Congress of Allergy, London, England, Sept. 2-4. For information address: British Association of Allergists, Write-Fleming Institute, St. Mary's Hospital, London, W. 2, England.

European Congress of Rheumatism, Istanbul, Turkey, Sept. 18-21. For information address: Professor Hami Kocas, Medical School, Ankara, Turkey.

European Society of Haematology (Seventh Congress), Bedford College, London, Sept. 7-12. For information write: Dr. E. Neumark, Department of Pathology, St. Mary's Hospital, London, W. 2.

International Cardiovascular Society, Munich, Germany, Sept. 18-20. Dr. Henry Haimovici, 715 Park Ave., New York 21, Secretary-General.

International Congress of Air Pollution, New York City, Sept. 9-10. For information write: American Society for Mechanical Engineers, 29 W. 39th St., New York 18.

International Congress of Cancer Cytology, Madrid, Spain, Sept. 21-Oct. 3. For information write: Mrs. E. L. Maselli, P. O. Box 633, Coral Gables, Fla.

International Congress of Nephrology, Geneva, Switzerland, and Evian, France, Sept. 3-5. For information write: Dr. G. Richet, Hospital Necker, 149 rue de Sevres, Paris 7e, France.

International League Against Rheumatism, Istanbul, Turkey, Sept. 18-21. For information write: Prof. Hami Kocas, Medical School, Ankara, Turkey.

International Symposium on Anti-Infectious and Antimitotic Chemotherapy, Geneva, Switzerland, Sept. 12-13. For information write Dr. P. Rentchnick, Case Stand 471, Geneva, Switzerland.

International Tuberculosis Conference, Istanbul, Turkey, Sept. 11-18. Dr. T. I. Gokee, Selime Hatun, Mezarlik Sokak, Taksim, Istanbul, Turkey, Secretary-General.

International Union of the Medical Press, Cologne, Germany, Sept. 21-24. Dr. Stockhausen, Secretary of Bundesaerztekammer, Cologne, Germany.

World Congress for Physical Therapy, Paris, France, Sept. 6-12. For information write: Miss M. J. Neilson, Tavistock House, Tavistock Square, London, W. C. 1, England.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Congress of the French-Speaking Association of Pediatrics (17th), Montpellier, France, Oct. 12-14. Prof. Jean Captal, 2, Enclos Tissie Sarrus, Montpellier, France, Congress President.

International Congress of Therapeutics, Strasbourg, France, Oct. 19-31. For information write: Professor Fontaine, Doyen de la Faculte de Strasbourg, France, President.

November

Bahamas Medical Conference, British Colonial Hotel, Nassau, Nov. 27-Dec. 17. For information write: Dr. B. L. Frank, P. O. Box 4037, Fort Lauderdale, Fla.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines on medical subjects is published each week only for the information of readers of The Journal. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles reported.*

MAGAZINES

Consumer Bulletin, May, 1959

"Diet in Prevention of Degenerative Diseases."

The bulk of this report is a quote from an article in the *British Medical Journal,* by Dr. H. M. Sinclair, vice-president, Magdalen College, Oxford University. In discussing diet, Dr. Sinclair makes the following point: "I have for years carried on a lonely campaign against the overfeeding of children. In every animal in which the experiment has been made it has been shown that overfeeding during the period of growth and development shortens the period, so that adult size is reached earlier, and also shortens life. I believe this is a real danger in the U. S. A. and I believe we must also be careful lest by overfeeding children we hasten chronic degenerative diseases (such as heart disease, gallbladder disease, cancer, peptic ulcer, asthma, rheumatoid arthritis)."

Coronet, May, 1959

"Lose 4 Lbs. in 5 Days with the No-Hunger 1111 Diet," by Princess Alexandra Kropotkin.

The basic factors in this five-day diet are yoghurt and a 1,111 calorie per day intake of other foods.

"S.O.S. Surgeon." by George W. Herald.

The author tells the story of Dr. Guido Guida who, from Rome, Italy, offers seamen a round-the-clock first-aid service by short-wave radio. Dr. Guida and his colleagues broadcast medical advice for nonurgent cases four times a day and special broadcasts, including consultations with specialists, for emergency cases.

"The Clinic That Rebuilds Bodies," by Ralph Bass.

The author discusses the work being done by Dr. Howard Rusk and the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center.

Harper's Magazine, May, 1959

"Peering into the Smallest World," by Jack Long.

Mr. Long tells of the development and use of the electron microscope as a research tool. Capable of magnifying an object more than 300,000 times, the electron microscope can photograph an object 40 billionths of an inch wide or about a million times thinner than a single human hair. "Scientists agree," the article concludes, "that the greatest mystery which the electron microscope can help them solve is the basic life process of cell growth and change."

"Socialized Medicine, Ten Years Old," by Don Cook.

The author discusses the pros and cons of the British National Health Service, after 10 years of operation. He points out, "There are plenty of critics of the Health Service. There are doctors who are discouraged and bitter, and there are patients who complain loudly and frequently. There are individuals who would not dream of accepting free state medical treatment, and there are physicians who will have nothing to do with state-paid medical practice. But 'opponents' who would turn back the clock 10 years and return to the old medical system in this country are really non-existent." The major complaint he found among physicians was "the frivolous calls from patients." According to one English doctor, "Because a patient does not have to think twice about his condition, he is at the doctor constantly to do all sorts of things which would work out perfectly well by themselves. . . . This crowds the doctor's office and leads to very superficial examination . . . there is a tendency to have a quick look and then let the umbrella of antibiotic drugs take care of the rest."

Good Housekeeping, May, 1959

"I Live Each Day," by Booton Herndon.

This is the remarkable story of Mrs. Wenonah Chambers –she and five of her eight children are victims of muscular dystrophy. In addition to running her household, Mrs. Chambers serves as treasurer of the Atlanta Muscular Dystrophy Association and visits every one of the 125 patients in the area regularly.

"Our Cruel Problems with Old Folks at Home," by Robert J. Levin.

The article discusses the problems faced by aging parents and their adult married children. Proper housing facilities, the author believes, is one of the most pressing problems faced by the aged, and he cites critic Louis Mumford: "Probably at no period and in no culture have the old ever been so completely rejected as in our own country, during the last generation."

Saturday Evening Post, April 25, 1959

"The Source of the Trouble," by Milton Silverman.

The last article in this three-part series on malpractice looks into the "suit-prone patient," hospital, and doctor. Mr. Silverman offers the following advice to physicians, based on an investigative report by the California Medical Association: "The doctor should look for signs of 'suit-proneness' in himself and in each of his patients. He should deal firmly with patient anger and understandingly with patient fear. If something goes wrong, he should sit down immediately and discuss the affair with the patient, understand and accept the emotional reactions of the patient and his family, be sympathetic and flexible and–when appropriate–be willing to adjust fees to 'fit family needs and medical realities.'

"'If such procedures are followed,' it was proposed, (in the CMA Report), 'one can estimate that two-thirds of unjustified suits now filed might be prevented.'"

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SOCIETY	PRESIDENT	SECRETARY	MEETING
American Public Health Association	Leona Baumgartner, New York City	Berwyn F. Mattison, 1790 Broadway, New York 19	Atlantic City, N. J., Oct. 19-23
Radium Society	Milford Schulz, Boston 14	Robert L. Brown, Robert Winship Clinic, Emory Univ., Atlanta, Ga.	
Rheumatism Assn.	James J. Bunim, Bethesda, Md.	Edward F. Hartung, 580 Park Ave., New York 21	Washington, D. C., June 2-6
Roentgen Ray Society	Barton R. Young, Philadelphia	C. Allen Good, 200 1st St., S.W., Rochester, Minn.	Cincinnati, Sept. 22-25
School Health Assn.	Delbert Oberteuffer, Columbus, Ohio	A. O. DeWeese, 515 E. Main St., Kent, Ohio	Atlantic City, N. J., Oct. 18-23
Society for Clinical Investigation	John A. Leutscher, Jr., San Francisco	S. J. Farber, 550 1st Ave., New York 16	
Society for Experimental Pathology	W. B. Wartman, Chicago	J. F. A. McManus, Univ. of Ala. Med. Center, Birmingham, Ala.	
Society for Pharm. & Ex. Ther.	Chauncey Leake, Columbus 16	Harold Hodge, Univ. of Rochester, Rochester 20, N. Y.	Cincinnati, Apr. 1-3
Society for the Study of Sterility	Charles Lee Buxton, New Haven, Conn.	H. H. Thomas, 920 S. 19th St., Birmingham, Ala.	Bal Harbour, Fla., Oct. 5-9
Society of Anesthesiologists	Daniel C. Moore, Seattle 1	J. E. Remlinger, 802 Ashland Ave., Wilmette, Ill.	
Society of Biological Chemists	S. Ochoa, New York	Philip Handler, Duke University, Durham, N. C.	Chicago, Sept. 7-11
Society of Clinical Pathologists	Edward L. Burns, Toledo, Ohio	Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14	
Society of Maxillofacial Surgeons	F. S. Dunn, New York 21	Orion H. Stuteville, 700 N. Michigan Ave., Chicago 11	Miami Beach, Fla., Oct. 18-23
Society of Plastic & Reconst. Surg.	Louis T. Byars, St. Louis 8	Thomas R. Broadbent, 508 E. S. Temple, Salt Lake City	Indianapolis, Oct. 28-31
Society of Tropical Medicine & Hygiene	Lewis W. Hackett, Berkeley, Calif.	R. B. Hill, 3575 St. Gaudens Rd., Miami 33, Fla.	Atlantic City, N. J., '59
Surgical Assn.	I. S. Ravdin, Philadelphia	W. A. Altemeier, Cincinnati Gen. Hosp., Cincinnati 29	Atlantic City, N. J., June 4-7
Therapeutic Society	Tom D. Spies, Birmingham, Ala.	O. B. Hunter, Jr., 915 19th St., N.W., Washington, D.C.	
Trudeau Society	Daniel E. Jenkins, Houston, Tex.	E. P. K. Fenger, 1790 Broadway, New York 19	
Urological Assn.	Adolph Kutzmann, Los Angeles 57	Samuel L. Raines, 188 S. Bellevue Blvd., Memphis, Tenn.	
Venereal Disease Assn.	Sidney Olansky, Durham, N. C.	S. R. Taggart, 1325 Upshur St., N.W., Wash., D. C.	Kansas City, Mo., Aug. 24-28
Veterinary Medical Assn.	R. E. Rebrassier, Columbus, Ohio	H. E. Kingman Jr., 600 S. Michigan Ave., Chicago 5	
Assn. for Research in Nervous & Ment. Dis.	Lee Eaton, Rochester, Minn.	Rollo J. Masselink, 700 W. 168th St., New York 32	
Assn. for Research in Ophthalmology	Hunter H. Romaine, New York 21	Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6	Atlantic City, N. J., June 8-12
Assn. of American Medical Colleges	John McK. Mitchell, Philadelphia	Richard H. Young, 2530 Ridge Ave., Evanston, Ill.	Chicago, Nov. 2-4
Assn. of American Physicians	Walter Bauer, New Haven 11, Conn.	P. B. Beeson, Yale U. Sch. of Med., New Haven 11, Conn.	Atlantic City, N. J., May 5-6
Assn. of Life Ins. Med. Dir. of America	Henry B. Kirkland, Newark, N. J.	Royal S. Schaaf, P. O. Box 594, Newark 1, N. J.	New York City, Oct. 21-23
Assn. of Medical Illustrators	Miss Kay Hyde, San Francisco 21	Miss Rose M. Reynolds, 42nd and Dewey Ave., Omaha 5	Seattle, Oct. 5-7
Assn. of Military Surgeons of U. S.	Brig. Gen. H. H. Twitchell, APO 633, New York City	R. E. Bitner, 1726 I St., N.W., Washington 6, D. C.	Washington, D. C., Nov. 8-11
Assn. of Public Health Phys.	Sanford P. Lehman, Seattle	Joseph M. Bistowish, P. O. Box 1117, Tallahassee, Fla.	
Assn. of State & Territorial Health Officers	D. G. Gill, Montgomery, Ala.	M. F. Shanholtz, State Office Bldg., Richmond, Va.	Washington, D. C.
Biological Photographic Assn.	Mr. Leo C. Massopust, Milwaukee	Miss J. Waters, Box 1668, Grand Central P. O., N. Y. 17	Montreal, Canada, Aug. 31-Sept. 3
Central Assn. of Ob. & Gyn.	Axel N. Arneson, St. Louis 8	Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3	Chicago, Sept. 24-26
Central Neuropsychiatric Assn.	Hamilton Ford, Galveston, Texas	R. M. Patterson, Ohio S. Univ. Col. of Med., Columbus 10, Ohio	New Orleans, Oct. 16-17
Central Society for Clinical Research	Edgar S. Gordon, Madison 6, Wis.	Austin S. Weisburger, 2065 Adelbert Rd., Cleveland 6	Chicago, Nov. 6-7
Central Surgical Assn.	Charles D. Branch, Peoria, Ill.	A. D. McLachlin, Victoria Hosp., London, Ont., Canada	Chicago, Feb. 18-20
Clinical Orthopaedic Society	Marcus J. Stewart, Memphis 5, Tenn.	Charles H. Frantz, 1810 Wealthy St. S.E., Grand Rapids, Mich.	
College of American Pathologists	Charles P. Larson, Tacoma, Wash.	A. H. Dearing, Prudential Plaza, Suite 2115, Chicago 1	Chicago, Sept. 6
Gerontological Society	Mr. Louis Kuplan, Sacramento, Calif.	Robert W. Kleemeier, St. Louis	Detroit, Nov. 12-14
Industrial Medical Association	H. W. Lawrence, Cincinnati 17	Leonard Arling, 3101 Univ. Ave., S.E., Minneapolis 14	
Interstate Postgrad. Med. Assn. of N. A.	Samuel Marshall, Boston	Erwin R. Schmidt, Box 1109, Madison 1, Wis.	Chicago, Nov. 2-5
Medical Library Assn.	Miss Isabelle Anderson, Denver	Mrs. H. T. Perkins, 333 Cedar St., New Haven 11, Conn.	
National Medical Assn.	S. Stillman Smith, Macon, Ga.	John T. Givens, 1108 Church St., Norfolk 10, Va.	Detroit, Aug. 10-13
National Multiple Sclerosis Society	Mr. Ralph C. Glock, New York	Mr. Donald Vail, 257 Fourth Ave., New York 10	New York, Mar. 8
National Proctologic Assn.	Peggy Cornet, Chicago Heights, Ill.	George E. Mueller, 59 E. Madison St., Chicago 2	Chicago, Nov. '59
National Tuberculosis Assn.	Mario Fischer, New York 19	Mrs. Wallace B. White, 1790 Broadway, New York 19	Chicago, May 24-29
Neurosurgical Society of America	Collin S. MacCarty, Rochester, Minn.	Raymond K. Thompson, 803 Cathedral St., Baltimore 1	Del Monte Lodge, Calif., Mar. 30-Apr. 2
Radiological Society of North America	Laurence L. Robbins, Boston 14	D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y.	Chicago, Nov. 15-20
Society for Investigate Dermatology	Walter C. Lobitz Jr., Hanover, N.H.	Herman Beerman, 255 S. 17th St., Philadelphia 3	
Society for Pediatric Research	Sydney S. Gellis, Boston	Clark D. West, Children's Hosp., Cincinnati	Buck Hill Falls, Pa., May 8-9
Society for Vascular Surgery	Arthur H. Blakemore, New York 32	Henry Swan, 4200 East 9th Ave., Denver 20	
Society of American Bacteriologists	Harry Eagle, Bethesda, Md.	E. M. Foster, Univ. of Wisconsin, Madison 6, Wis.	St. Louis, May 10-15
Society of Biological Psychiatry	Joseph Wortis, Brooklyn, N. Y.	George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57	Atlantic City, N. J., June 13-14
Society of Clinical Surgery	James Priestly, Rochester, Minn.	F. F. Albritten, Jr., Univ. of Kans., Kansas City, Kan.	
Society of Neurological Surgeons	Leonard T. Furlow, St. Louis 8	Bronson S. Ray, 525 E. 68th St., New York 21	
Society of University Surgeons	Henry T. Randall, New York 21	Ben Eiseman, 4200 E. 9th Ave., Denver 20	Minneapolis, Feb. 11-13
Southeastern Surgical Congress	B. T. Beasley, Atlanta, Ga.	B. T. Beasley, 45 Edgewood Ave. S.E., Atlanta 3, Ga.	New Orleans, Mar. 31-34
Southern Medical Assn.	Milford O. Rouse, Dallas 1, Texas	Mr. V. O. Forter, 2601 Highland Ave., Birmingham 5, Ala.	Atlanta, Ga., Nov. 16-19
Southern Surgical Assn.	James D. Rives, New Orleans 12, La.	George G. Finney, 2947 St. Paul St., Baltimore 18	
Southwestern Medical Assn.	Louis G. Jekel, Phoenix, Ariz.	Russell L. Deter, 1501 Arizona St., El Paso, Tex.	
Southwestern Surgical Congress	Fred H. Krock, Fort Smith, Ark.	C. M. O'Leary, 1213 Med. Arts Bldg., Oklahoma City	Las Vegas, Nev., Mar. 29-31
Student American Medical Assn.	Mr. Carwile LeRoy, Chapel Hill, N. C.	Mr. Russell F. Staudacher, 430 N. Michigan, Chicago 11	Chicago, Apr. 30-May 3
The Endocrine Society	Leo T. Samuels, Salt Lake City	H. H. Turner, 1200 N. Walker St., Oklahoma City	
U. S. Section, Internat'l Coll. of Surgeons	Curtice Rosser, Dallas, Texas	Karl Meyer, 1516 Lake Shore Dr., Chicago	
Western Industrial Medical Assn.	Edward J. Zaik, Los Angeles 14	A. C. Remington, 9851 Sepulveda Blvd., Los Angeles 45	Los Angeles, Oct. 2-3
Western Orthopedic Assn.	William F. Stanek, Denver 6	Miss Vi Mathiesen, 354-21st St., Oakland 12, Calif.	Denver, Oct. 18-22
Western Society of Electro-Encephalography	Donald B. Lindsley, Los Angeles 24	Kenneth A. Blinn, 4120 Atlantic Ave., Long Beach, Calif.	
Western Surgical Assn.	James T. Priestley, Rochester, Minn.	John T. Reynolds, 612 N. Michigan Blvd., Chicago 11	Colorado Springs, Colo., Nov. 19-21
Woman's Auxiliary to the Am. Med. Assn.	E. Arthur Underwood, Vancouver, Wash.	Miss Margaret Wolfe, 535 N. Dearborn St., Chicago 10	Atlantic City, N. J., June 8-12
World Medical Assn.	Charles Jacobsen, Denmark	Louis H. Bauer, 10 Columbus Circle, New York 19	Montreal, Canada, Sept. 7-12

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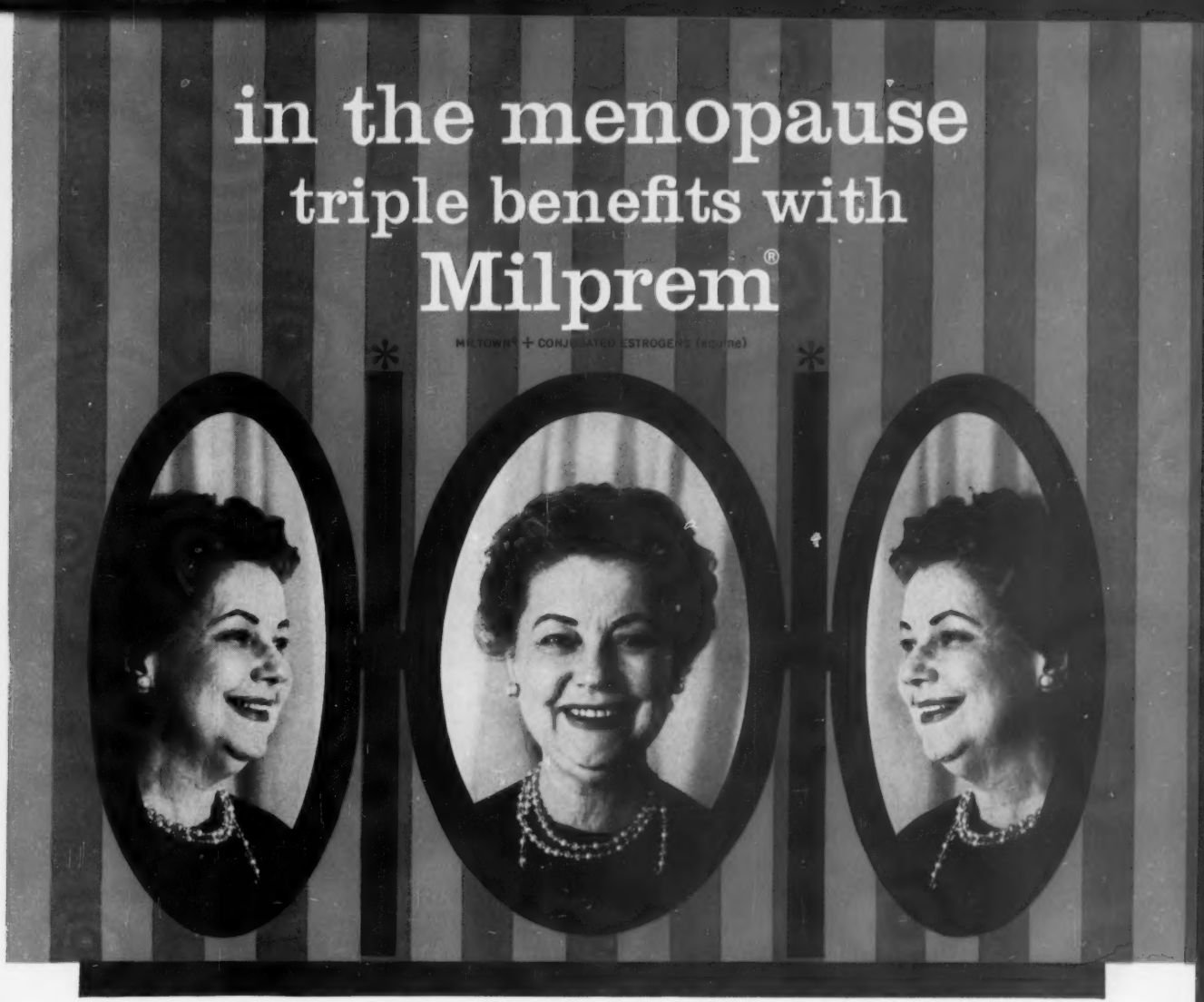

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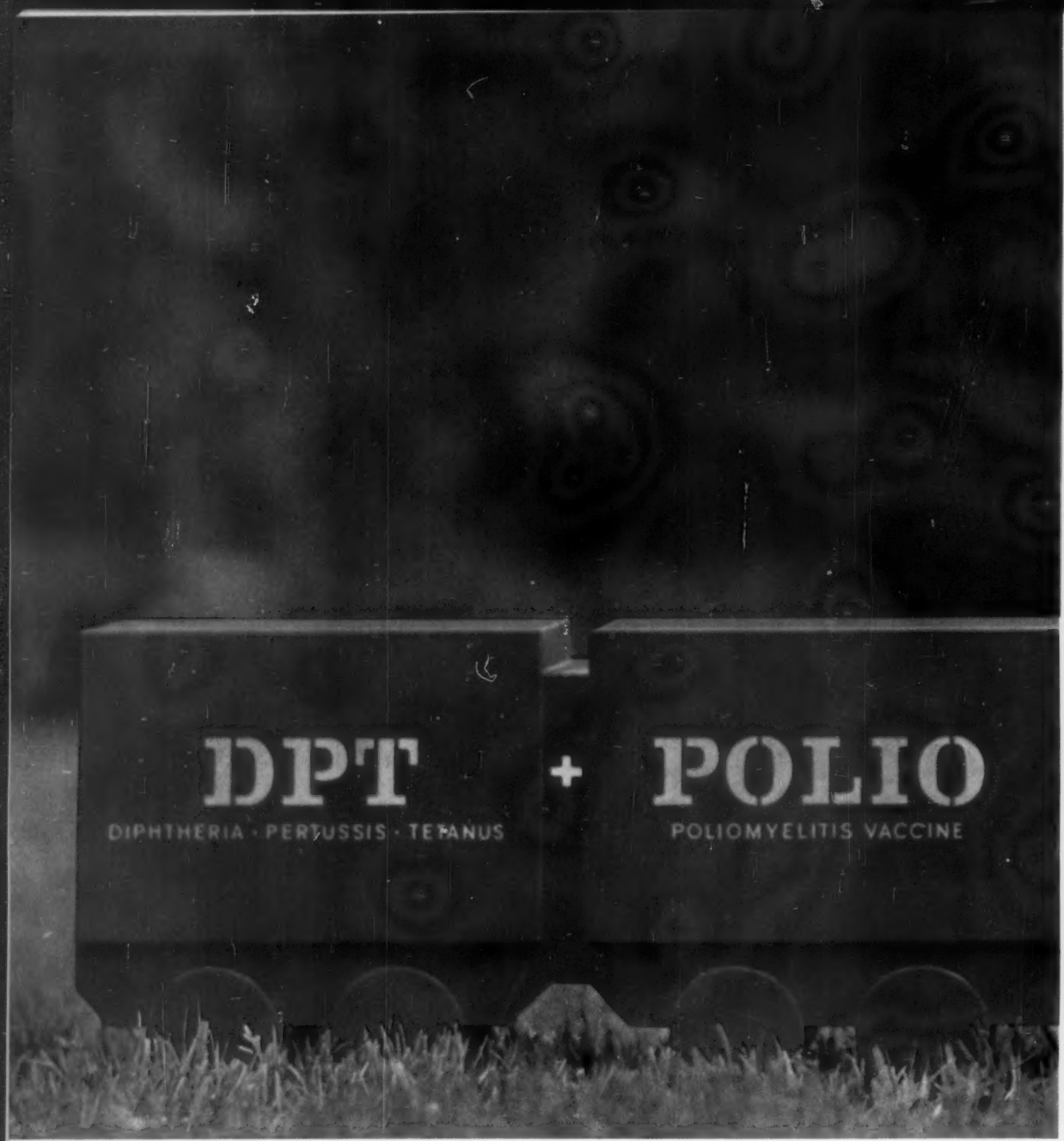

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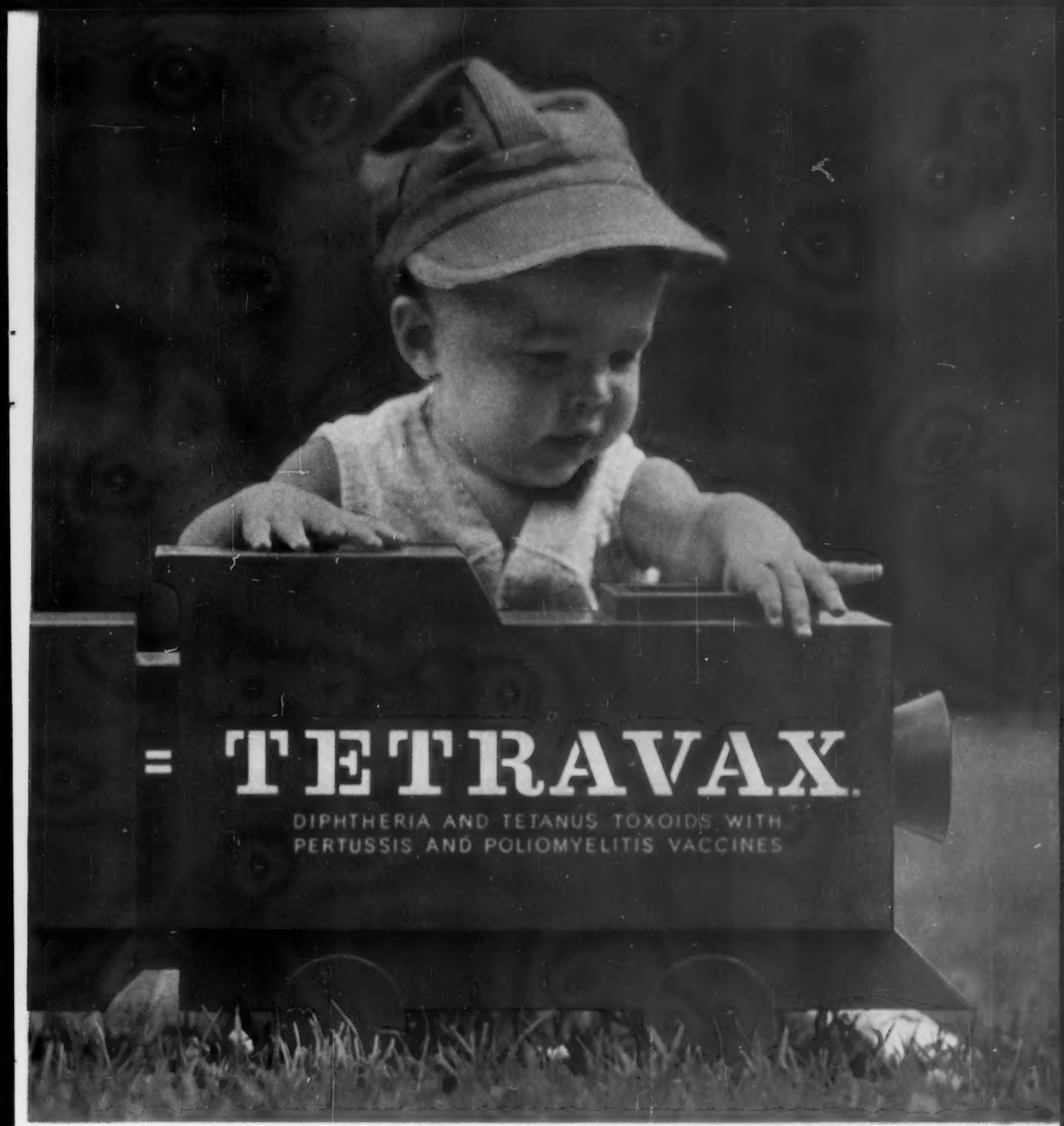

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Reinhardt, D. J.:
Delaware State Med. J. **30**:1, January 1958.

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Bunn, W. H., Jr.:
Ohio State Med. J. **54**:1168, September 1958.

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*Freis, E. D., *et al.*: Treatment of Essential Hypertension with Chlorothiazide (DIURIL), J. A. M. A. **166**: 137, Jan. 11, 1958.

Reinhardt, D. J.: The Impact of Chlorothiazide (DIURIL) on Therapy in Arterial Hypertension, Delaware M. J. **30: 1, Jan. 1958.

***Landes, R. P., and Peters, M.: Clinical Observations on Chlorothiazide, Postgraduate Medicine **23**: 648, June 1958.

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SCIENTIFIC PROGRAM

First Scientific Session — Friday, June 5 — 9:00 A.M. — 12:30 P.M.

MODERN CONCEPTS IN ANGIOLOGY
J. E. Estes, M.D., Mayo Clinic, Rochester, Minnesota, Moderator

THE MICRO-CIRCULATION
G. P. Fulton, Ph.D., Professor of Biology, Boston University, Boston, Mass.

THE NATURAL HISTORY OF ATHEROSCLEROSIS OF THE LOWER EXTREMITIES
A. M. Boyd, M.D., Professor, Univ. of Manchester, Manchester, England.

FUNCTIONAL PULMONARY VASCULAR DISTURBANCES AND THE RELATION TO PULMONARY HYPERTENSION
M. Hochrein, M.D., Professor of Medicine, Heidelberg University, Ludwigshafen, Germany.

SEROTONIN AND THE VASCULAR SYSTEM
F. J. Haddy, M.D., Ph.D., Dept. of Physiology, Northwestern Univ. School of Medicine, Veterans Administration Research Hospital, Chicago, Illinois.

RAYNAUD'S DISEASE, RAYNAUD'S PHENOMENON AND SEROTONIN
P. H. Kuhn, M.D., Assistant Professor of Clinical Medicine, New York University Postgraduate Medical School and A. Halpern, Ph.D., Director, Department of Experimental Therapy, Stuyvesant Polyclinic, New York.

STRESS, SEMANTICS AND THE VASCULAR SYSTEM
A. M. Ostfeld, M.D., Assistant Professor, University of Illinois, College of Medicine, Chicago, Illinois.

STRESS AND CARDIAC INFARCTS
H. Selye, M.D., Professor and Director, Institute of Experimental Medicine and Surgery, University of Montreal, Montreal, Canada.

PANEL DISCUSSION — QUESTIONS AND ANSWERS

Second Scientific Session — Friday, June 5 — 2:00 P.M. — 5:00 P.M.

NEWER APPROACHES TO PERIPHERAL VASCULAR DISEASE
R. W. Gifford, Jr., M.D., Mayo Clinic, Rochester, Minnesota, Moderator

VASCULAR COMPLICATIONS OF ORTHOPEDIC CONDITIONS AT VARIOUS AGES
D. S. Miller, M.D., Professor and Chairman, Department of Orthopedic Surgery, Chicago Medical School and Cook County Graduate School of Medicine, Chicago, Illinois.

HISTANGIC CONNECTION IN THE PHLEBOPATHIC ULCERS OF THE LEG
M. Comel, M.D., Professor, University of Pisa and Director, Athenseum Angiologicum Santorianum, Pisa, Italy, President, International Union of Angiology, Paris, France.

COCKETT'S OPERATION AND/OR POPLITEAL RESECTION IN THE TREATMENT OF LEG ULCERS
G. Bauer, M.D., Professor, General Hospital, Mariestad, Sweden.

SERIAL ANGIOGRAPHY AND THE DIAGNOSIS OF PERIPHERAL VASCULAR DISEASE
H. W. Paessler, M.D., Medical Director and Chief Physician of the Surgical Clinic, State Hospital, Leverkusen, Germany.

SCLEROSING AORTITIS AND ARTERITIS WITH NARROWING AND OCCLUSION OF THE MAJOR BRANCHES OF THE AORTA (PULSELESS DISEASE)
S. W. Czarnecki, Captain, M.C., W. C. Manion, M.D. and T. W. Mattingly, M.D., Walter Reed Hospital and Washington Hospital Center, Washington, D. C.

THE ROLE OF FIBRINOLYTIC AGENTS IN THROMBOTIC DISEASES
R. V. Chapple, M.D. and H. O. Singher, Ph.D., Ortho Research Foundation, New Jersey.

PERIPHERAL VASODILATION: METHODS OF EVALUATION AND THE CORRELATION WITH CLINICAL PRACTICE
F. Kaindl, M.D., Professor, University of Vienna, Vienna, Austria.

GANGRENE IN THE AGED
S. S. Samuels, M.D. and H. E. Shaftel, M.D., Dept. of Experimental Angiology, Stuyvesant Polyclinic and The Angiology Research Foundation, New York.

PANEL DISCUSSION — QUESTIONS AND ANSWERS

Third Scientific Session — Saturday, June 6 — 9:00 A.M. — 12:30 P.M.

RECENT ADVANCES IN SURGERY OF THE HEART AND ARTERIES
C. A. Hufnagel, M.D., Professor of Surgical Research, Associate Professor of Surgery, Georgetown University, Washington, D. C., Moderator

CORONARY ARTERIOGRAPHY: A NEW METHOD
G. Arnulf, M.D., Professor of Surgery, University of Lyons, Lyons, France.

CARDIOPLEGIA — EXPERIMENTAL AND CLINICAL
C. A. Hufnagel, M.D., Professor of Surgical Research, Associate Professor of Surgery, Georgetown University, Washington, D. C.

THE USE OF CARDIOPULMONARY BY-PASS FOR CONGENITAL AND ACQUIRED LESIONS OF THE HEART
A. A. Bakst, M.D., and L. Loewe, M.D., Downstate Medical Center, State University of New York, Brooklyn Jewish Hospital, Brooklyn, New York.

RECONSTRUCTIVE SURGERY IN PERIPHERAL ARTERIAL OBLITERATION
R. Fontaine, M.D., Professor of Surgery, University of Strasbourg, Strasbourg, France.

SURGERY FOR COARCTATION OF THE AORTA
A. R. Albanese, M.D., Professor, Univ. of Argentina, Buenos Aires, Arg.

THE SURGERY OF VASOSPASTIC ARTERIAL DISEASE
E. Malan, M.D., Professor of Surgery, University of Genoa, Genoa, Italy.

PANEL DISCUSSION — QUESTIONS AND ANSWERS

Fourth Scientific Session — Saturday, June 6 — 2:00 P.M. — 5:00 P.M.

NEWER ASPECTS OF THROMBOEMBOLIC DISEASE AND INTRAVASCULAR PHENOMENA
T. W. Mattingly, M.D., Director of Medical Education, Washington Hospital Center, Washington, D. C., Moderator

THE PHYSIOLOGIC PROTECTIVE MECHANISMS AGAINST INTRAVASCULAR CLOTTING
A. J. Quick, M.D., Professor, Biochemistry, Marquette University Medical School, Milwaukee, Wisconsin.

RELATIONSHIP OF THE ORAL ANTICOAGULANTS TO THE BLOOD COAGULATION MECHANISM
S. A. Johnson, Ph.D., Henry Ford Hospital, Detroit, Michigan.

BLOOD SLUDGING
M. H. Knisely, Ph.D., Professor and Chairman, Department of Anatomy, Medical College of South Carolina, Charleston, South Carolina

THE FIBRINOLYTIC SYSTEM
T. Astrup, M.D., Biological Institute, Copenhagen, Denmark

CREPUSCULAR THROMBOEMBOLIC SYNDROMES
A. B. Hagedorn, M.D., Dept. of Medicine, Mayo Clinic, Rochester, Minn.

PANEL DISCUSSION — QUESTIONS AND ANSWERS

Fifth Scientific Session — Sunday, June 7 — 10:00 A.M. — 12:00 P.M.

A CLINICO-PATHOLOGIC CONFERENCE: INTRATHORACIC PROBLEMS
J. E. Edwards, M.D., Mayo Clinic, Rochester, Minnesota, Moderator

Panelists: R. G. Lester, Department of Radiology, University of Minnesota, Minneapolis, Minnesota. • R. P. Glover, M.D., Director, Cardiovascular Research Laboratory and Chief of Thoracic and Cardiac Surgery, Presbyterian Hospital, Philadelphia, Pennsylvania. • R. S. Ross, M.D., Department of Medicine, Johns Hopkins Hospital, Baltimore, Maryland.

Sixth Scientific Session — Sunday, June 7 — 2:00 P.M. — 4:00 P.M.

EXPERIMENTAL ANGIOLOGY
D. W. Kramer, M.D., Professor, Jefferson Medical School, Philadelphia, Pennsylvania, Moderator

A series of original reports of experimental and clinical research in Angiology. Presentations are limited to 15 minutes. Presentations limited to those by Fellows of the College.

Round-Table Luncheons

Round-table luncheons will be held Friday and Saturday on selected subjects. For listing and reservations, write to: Alfred Halpern, Ph.D., F.A.C.A., American College of Angiology, 11 Hampton Court, Great Neck, N. Y.

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References: 1. Graham, W.: Canad. M. A. J. 79:634 (Oct. 15) 1958. 2. Robins, H. M.; Lockie, L. M.; Norcross, B.; Latona, S., and Riordan, D. J.: Am. Pract. Digest Treat. 8:1758, 1957. 3. Kuzell, W. C.; Schaffarzick, R. W.; Naugler, W. E., and Champlin, B. M.: New England J. Med. 256:388, 1957.

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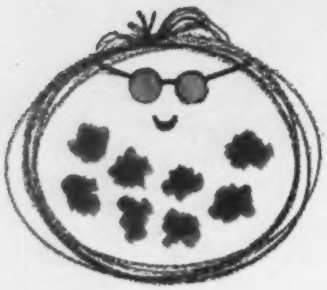

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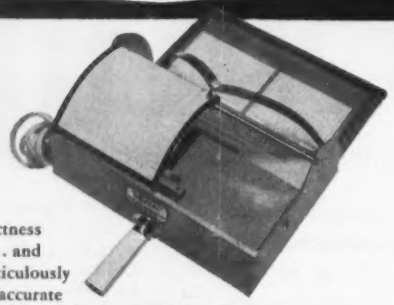

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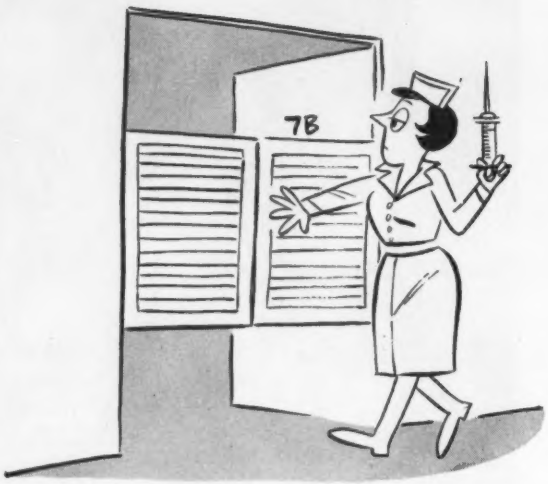

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	Calories from Fat	Calories from Protein
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in pork loin chop (lean portion only)	1	1.36
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*Leverton, R.: The Fat, Protein, and Calorie Value of Cooked Meats. Proc. 9th Research Conf. sponsored by the Council on Research of the American Meat Institute, University of Chicago, March 1957.

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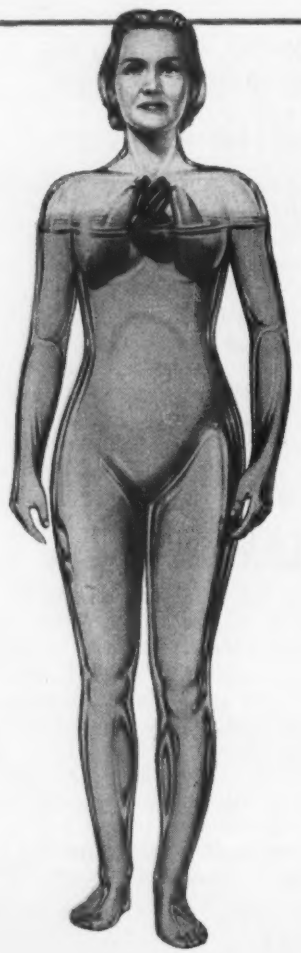

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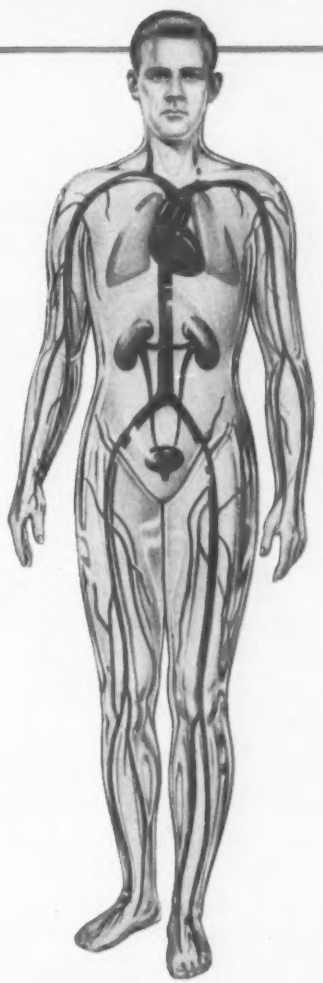

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FROM OTHER PAGES

Balance in Education

There are three senses in which we might consider balance in education. The first arises from two different conceptions of the purpose of education. On the one hand there is the formation of character, and the development of intellect and personality. At the other extreme is the concept which I suppose finds its most powerful expression in the educational philosophy of Soviet Russia, that the purpose of education is to provide useful members of society in which the desires of the individual must be subordinated to the needs of society. I do not believe that these two concepts are wholly conflicting nor that the second runs completely counter to the British tradition of individual liberty. A balanced educational system should have room for both. The striking successes achieved by the Russians in science and technology are directly attributable to a system of education deliberately designed to produce large numbers of technically trained men and women with the ability to increase the economic power of the country through industrialization. . . . We are proud that our universities, . . . still retain their academic independence intact. Nevertheless, they have quite properly reacted to the stimulus of the country's needs which have led the older universities, for so long the home of the humanities, themselves to enlarge their science faculties. So, in framing our formal education, we cannot entirely ignore the requirements of the society on whose prosperity depend the very conditions in which our educational system can progress; but our society will not be tolerable to live in if its members are not permitted to develop their personalities and talents.

This brings me to the second sense in which I refer to balance in education. I am thinking here of the need for those who study the humanities to have some understanding of the workings of science, and for our scientists to widen their horizons by relating their science to its human context both historically and in terms of the present day. . . . The gulf which at present separates our scientists and non-scientists, is much more easily bridged than is often imagined. For example, the qualities of mind which are fostered by studying chemistry and history are very much alike. Both chemists and historians must cultivate an inquisitive and acquisitive mind. Both need to exercise judgment, leavened with a good measure of scepticism in the exemplary tradition of Robert Boyle. Both must be imaginative. . . .

There is a third and final sense in which I refer to balance in education. I have said that we demand, from our scientists and non-scientists alike, intellectual qualities, such as curiosity, judgment and imagination. Equally we want our young people, whatever their branch of study, to possess high qualities of character. I need not enlarge on this theme to say that the society which a balanced partnership of science and business can help to build, will as always call for courage, integrity and tenacity. These are some of the ideals that we might have in our minds, as we each address ourselves to the problems of education for an age of science.—

Sir Alexander Fleck, K.B.E., F.R.S., Science and Business: A Balanced Partnership, *The Pharmaceutical Journal*, Sept. 6, 1958.

A Belated Tribute to Some Friends of Medicine

This brief article is . . . to remind the medical profession of . . . enthusiastic supporters of individual physicians and the private practice of medicine in the United States today. . . .

The average funeral director has gradually accepted more and more of the role of comforting a family in their bereavement. . . . Many funeral directors insist that this is the most important single service which they render and it certainly should be said that it is the one most often appreciated by the family. Another service which the funeral director provides for the average family is a source of temporary funds in cases of emergency. Few professional or businessmen realize the huge cash outlays that the average funeral director makes in advance for a funeral in purchasing services which must be paid immediately. Since it is very unusual for a funeral director to be paid in advance or even at the time of the funeral, he often has very large accounts receivable and often advances relatively large sums of money to families for transportation and similar expenses incurred in association with a death. . . . Considering the funeral directors as individuals, only the family's pastor is invited to help more at the time of bereavement by a family. . . .

In addition to the assistance which physicians receive in association with the management of a family during the time of bereavement, there are two technical aspects of medicine in which the funeral director's assistance is indispensable. The first of these is the service which the funeral directors have undertaken in the preparation of death certificates. Although this responsibility has been placed upon them by the state, it would seem that they have accepted it more voluntarily and that they might be able to reverse this responsibility if the burden ever becomes too difficult to bear. Ordinarily the funeral director personally sees to it that the physician has signed a death certificate before the body is buried. This is not always an easy responsibility. . . .

My work as a pathologist makes me far more aware and far more impressed by the willingness of most modern funeral directors to encourage the advancement of medical science by assisting with the obtaining of autopsy permits than perhaps, is the average physician. The professional funeral director realizes that the physician's knowledge of medicine will be greatly helped by postmortem examination, in those patients in whom therapy is a failure. It is a sign of the real sacrifice which is expected of (and assumed by) professional people that funeral directors will rearrange their own time schedules, delay their technical preparation of the body, and deliver bodies over relatively long distances (which costs them at least 20 cents per mile) in order to assist the performance of an autopsy. When approached by a physician who needs assistance, most will do everything in their power to urge a family to permit a postmortem examination. Without question this assistance has increased the autopsy rate in our community by at least 10% and probably considerably more. —J. D. MacCarthy, M.D., A Belated Tribute to Some Friends of Medicine, *Bulletin of the Spokane County Medical Society*, September, 1958.

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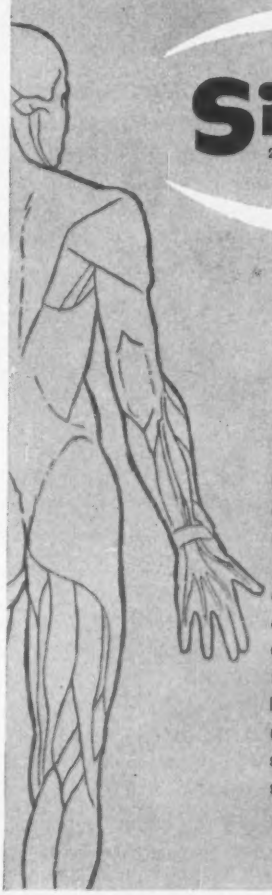

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Supplied: 200 mg. tablets in bottles of 50.

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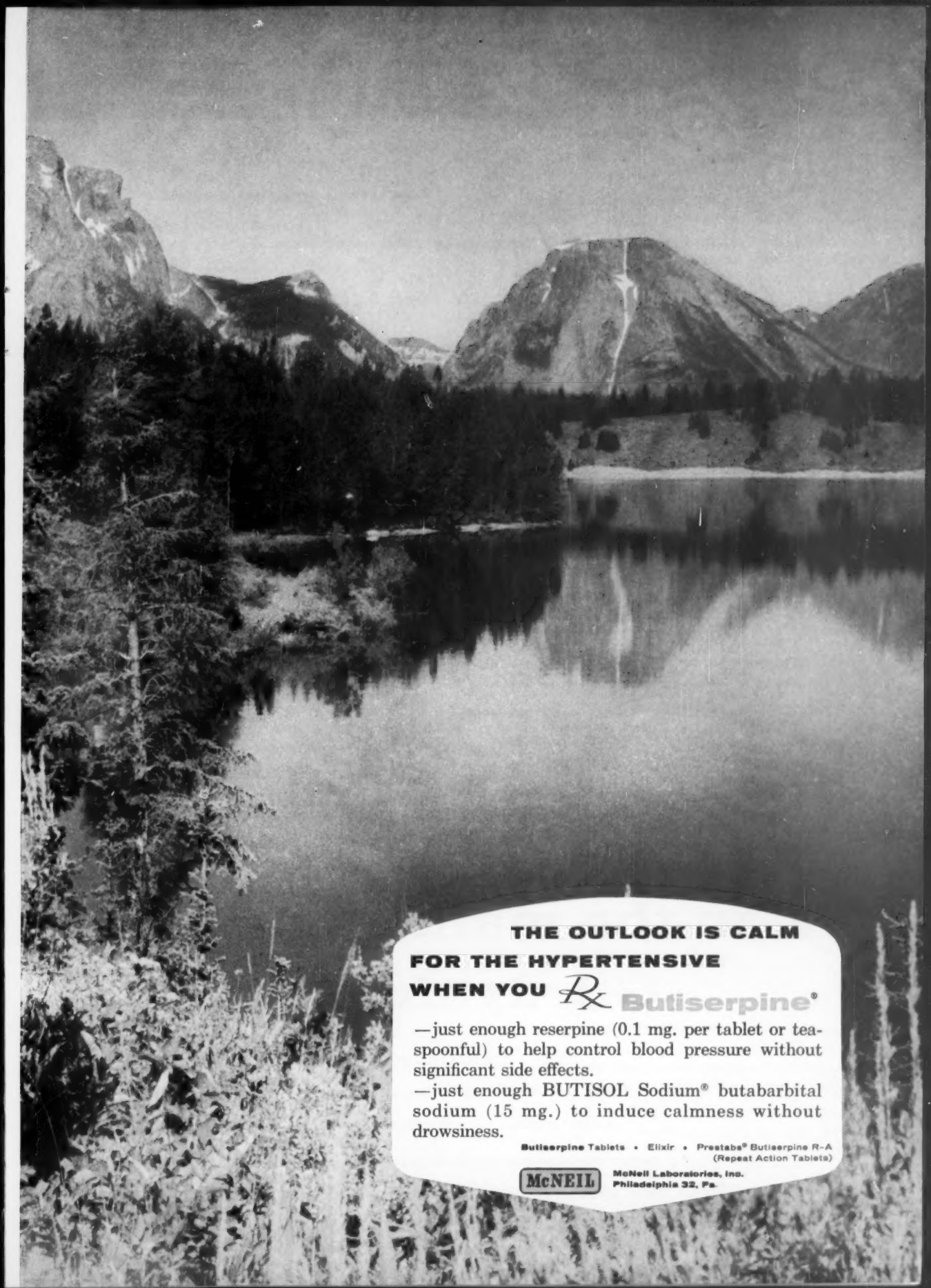
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in the management of G.I. dysfunction

INDICATIONS: duodenal and gastric ulcer • colitis spastic and irritable colon • gastric hypermotility • gastritis • esophageal spasm • intestinal colic • functional diarrhea • G. I. symptoms of anxiety states.

FORMULA: each scored tablet contains: meprobamate 400 mg., tridihexethyl chloride 25 mg. *(formerly supplied as the iodide)*

DOSAGE: 1 tablet t.i.d. with meals and 2 tablets at bedtime.

REPORTED FROM	NO. OF CASES	DIAGNOSES	RESULTS	SIDE EFFECTS	CONCLUSIONS
Texas	9	1 gastritis, 1 spastic enterocolitis, 2 spastic duodenitis, 1 duodenal ulcer, 1 G.I. symptoms of anxiety state, 1 gastric ulcer, 1 duodenal ulcer with pinpoint perforation-chronic, 1 cardiac neurosis with G.I. symptoms.	Marked improvement (9)	None (7) Drowsiness (1) Initial drowsiness (1)	4–excellent results, 1–good, 1–fine, 1-6 weeks' x-ray showed G.I. crater filled in and asymptomatic: tension disappeared, 1–symptoms completely ameliorated. 1–complete relief: on Milpath since the day it came out.
Ohio	15	7 G.I. symptoms of anxiety states, 4 duodenal ulcer, 2 spastic colon, 1 colitis-catarrhal, 1 diverticulosis.	Much improvement (1) Marked improvement (9) Slight improvement (4) Variable (1)	None (11) No answer (2) "Floating sensation" (1) Transient "lightheaded" feeling (1)	1–improvement over previous treatment, 2–well pleased, 1–was striking, 1–quite satisfied, 1–good, 1–was grateful, 1–better than previous regimen, 1–indefinite, 2–very satisfactory, 1–undecided, 1–excellent, 1–"patient as well as myself was much impressed," 1–"Milpath therapy should be continued inasmuch as he has had ailment so long."
California	4	3 G.I. symptoms of anxiety states, 1 duodenal ulcer.	Marked improvement (3) Slight improvement (1)	None (4)	1–good, 3–satisfactory (1–continuing on decreasing dosage).
Idaho	5	1 gastro-enteritis of late pregnancy, 1 gastritis of late pregnancy, 1 chronic duodenal ulcer, 1 functional upper G.I. tract disease, 1 chronic gastro-duodenitis.	Marked improvement (5)	None (2) None of significance (2) Minimal drowsiness (1)	3–very effective, 1–believed to be of significant merit for upper G.I. distress of late pregnancy, 1–one of the most effective medications used to date.
Illinois	5	2 hyperacidity, 3 peptic ulcer.	Marked improvement (5)	None (5)	2–excellent, 2–very good auxiliary treatment; 1–"of great importance in treatment of peptic ulcer."
Missouri	1	Pylorospasm.	Marked improvement	None	Effective G.I. antispasmodic.
North Carolina	15	10 pylorospasm, 2 duodenal ulcer, 1 possible Ca. of G.I. tract, 1 G.I. symptoms of anxiety, 1 gastritis–(alcoholic).	Marked improvement (11) Slight improvement (4)	None (14) Nausea (1)	12–very effective, 1–fairly good, 1–improved patient's condition, but did not solve the basic problem, 1–nausea (anomalous reaction).
Indiana	5	1 gastritis, 1 peptic ulcer (bleeding), 1 duodenal ulcer with gastritis, 1 duodenal ulcer, 1 psychoneurotic with gastric complications, insomnia.	Marked improvement (5)	None (3) Drowsiness (2)	1–excellent; patient has been feeling wonderful. 1–wonderful attitude on part of patient toward business life. 1–good, 2–excellent.
Oregon	10	3 gastritis, 2 spastic colitis, 3 G.I. symptoms of anxiety states, 1 healing duodenal ulcer, 1 herniation of pyloric mucosae.	Marked improvement (9) Slight improvement (1)	No side effects (6) Drowsiness (4)	9–very beneficial, 1–some improvement.
Florida	10	3 duodenal ulcer, 2 hypertrophic gastritis, 2 functional enterocolitis, 2 vomiting of pregnancy, 1 cardiospasm, menopausal syndrome.	Marked improvement (8) No improvement (2)	No side effects (9) Epigastric burning (1)	5–excellent, 1–no success, 3–very good, 1–inconclusive.
Michigan	10	1 spastic colitis, 2 gastrointestinal spasm, 1 colitis and diverticulitis, 1 duodenitis, 2 peptic ulcer, 2 duodenal ulcer, 1 gastric ulcer.	Marked improvement (8) Steady improvement (1) Slight improvement (1)	None (6) Some Dryness of Mouth (2) Drowsiness (2)	8–marked subjective and objective improvement, 1–encouraging improvement . . . patient has refused operation, so we are depending on this treatment, 1–steady improvement. Now on lower dosage and getting along well.

These evaluations are summary conclusions drawn from the continuing program of clinical research on Milpath in private practice.

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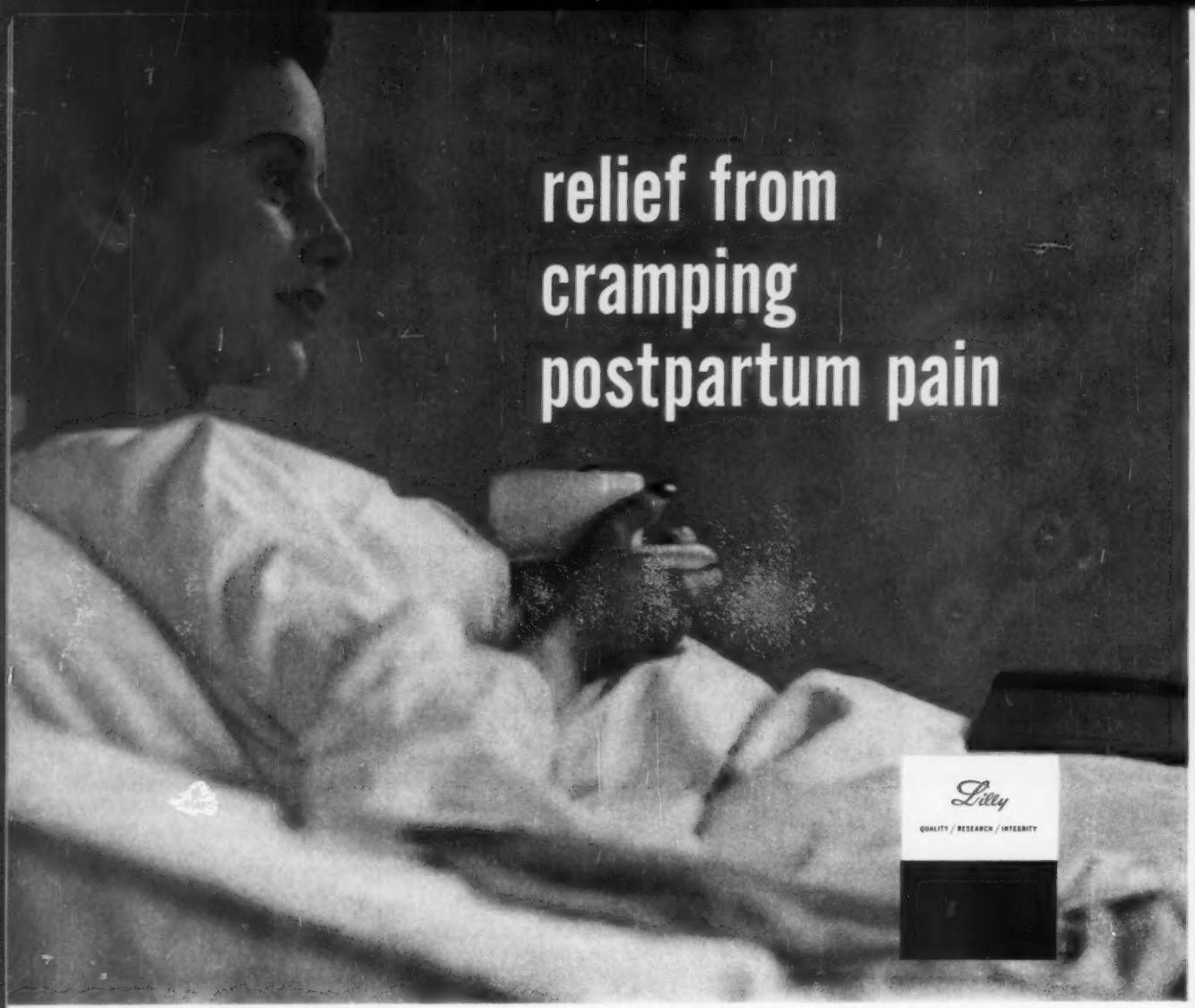
New Brunswick, N.J.



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ATTENUATED TYPE 1 POLIOVIRUS VACCINE

ITS CAPACITY TO INFECT AND TO SPREAD FROM "VACCINEES" WITHIN AN INSTITUTIONAL POPULATION

Dorothy M. Horstmann, M.D., James C. Niederman, M.D.
and
John R. Paul, M.D., New Haven, Conn.

Responses to the oral administration of Sabin's attenuated type 1 poliovirus vaccine were studied in a closed, institutional community under conditions that made it possible to compare individuals whose immunity had been acquired naturally with those who had received the Salk formalinized vaccine. The results showed that all infections induced by the vaccine were symptomless and that they spread readily through the small institutional community. The children whose antibodies had been acquired from the Salk vaccine were easily infected with the attenuated virus, whether they received it by mouth or through contact with individuals infected in the same cottage. In contrast, children whose antibodies had been acquired by previous natural infection were more resistant, but this depended somewhat on the dose of vaccine given. There were indications that passage of the virus through certain individuals slightly increased its neurotropism for the monkey.

THE GROUNDWORK for active immunization against poliomyelitis through the use of orally administered, live, attenuated poliovirus vaccines has been laid by Koprowski and co-workers [1] and Sabin.[2] Studies by Horstmann and associates [3] and Fox [4] have followed their lead. In expanding the trial use of such vaccines to determine further their value and limitations, certain procedures have been recommended by the World Health Organization's Expert Committee on Poliomyelitis.[5] There have been several trials aimed at testing the potentialities of these vaccines which either have been completed or are now in progress in Europe,[6] in the United States,[7] in Africa,[8] in South America,[9] in Russia, and elsewhere. Some have followed WHO recommendations, others have not.

Nevertheless, unanswered questions regarding the attenuated live poliovirus vaccines and their value continue to be numerous. These questions are related to their safety, their capacity to infect both the potential vaccinee and his intimate contacts, their immunogenic potency, and the possible indications for their use alone or in conjunction with the Salk (killed virus) vaccine.

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The present study conforms to WHO recommendations, and is concerned with some of these questions. Using Sabin's L Sc type 1 attenuated poliovirus, we have carried out three sequential trials in a closed, institutional community. The study population consisted of individuals with different types and levels of immunity, living in a special environment. Immediate objectives were to determine (1) whether children with some degree of immunity can be infected or reinfected with such an attenuated poliovirus, (2) whether there are differences in the responses to virus administration in children whose antibodies have been acquired from formalinized (Salk) vaccine as compared to those with naturally acquired antibodies to polioviruses, (3) the effect of dosage of attenuated poliovirus on its infective capacity, (4) the degree of spread of virus from inapparently infected vaccinees to their close associates, and (5) the effect of one or more human passages on the stability (avirulence) of the strain of type 1 poliovirus (L Sc) as it was excreted by infected individuals or by their contacts. Preliminary reports with regard to some of these five items have appeared.[3]

It turned out that in the course of the three trials we had a limited opportunity to watch an epidemic of inapparent infections start, grow, and terminate under controlled conditions. For, actually, what the artificial infection of a small population with live attenuated poliovirus may amount to is the induced spread of an infection which is not only harmless but should have a salutary immunizing effect on the hosts.

Plan of Trials

Study Population.—In each of the three trials, carried out in November, 1956, March 1957, and November, 1957, respectively, attenuated type 1 poliovirus was administered by mouth to selected children in a housing unit or cottage within an institution caring for adults and children. The unit chosen for the trials was divided into two sections which housed at the start 34 and 35 individuals respectively. Most of these were juveniles, but the age span ranged from 4 to 24 years. Up to 20 of these individuals were selected for virus feeding in any one of the three trials. All of the persons in the cottage were theoretically immune to paralytic poliomyelitis at the start of the first trial in November, 1956, i. e., they either had naturally acquired type 1 antibodies or had been vaccinated with Salk (killed virus) vaccine at least twice in the previous six months. In this sense each trial was one of bolstering already existing immunity.

Virus Administration and Laboratory Studies.—The L Sc strain of attenuated type 1 poliovirus which was used had been previously tested extensively in animals by Sabin,[2] who had also fed aliquots of the same lot to adult volunteers. This preparation had been purified by the terminal dilution method, rather than the plaque-purification method which has subsequently been adopted as the optimum method.[2]

The following schedule for the collection of specimens was used. After the administration of virus, daily throat swabs were taken for 10 days and daily stool collections for the first 2 weeks; then stool specimens weekly, and subsequently, at increasing intervals, for 56 to 70 days. Sequential blood specimens were collected before the virus feeding, and, beginning on the 7th day, at appropriate intervals up to the 56th day after ingestion of virus. A selected number of contacts of the live-virus vaccinees were followed similarly, and in the first trial, blood specimens were collected from the entire cottage population at the beginning and end of the trial.

Tissue cultures (trypsinized monkey kidney monolayers) were used for the detection and identification of poliovirus in throat swabs and stool specimens.[10] Antibody responses were measured by the colorimetric neutralization test in disposable plastic panels, and complement-fixation tests were performed on Lucite plates.[10]

First Trial—November, 1956

Twenty children were fed L Sc type 1 virus. Of these, 10 were in the (Salk) vaccine "immune" group, and have been designated as the (V) group, and 10 were in the naturally immune (N) group, those in each group being matched for age, so far as possible. It turned out that one child who was thought to have had low level natural antibody was in fact fully susceptible and reacted with a primary infection. The N group was thus reduced to nine children. The dose of virus fed to each of the 20 subjects was large: 1.0 ml. of tissue culture suspension containing approximately 25 million tissue culture infective doses ($10^{7.4}TCD_{50}$). In an attempt to bypass the throat, 7 individuals were fed this amount mixed with polyethylene glycol 400, in hard gelatin capsules; the other 13 children were given the same dose in liquid form in milk.

Prefeeding neutralizing antibodies in these children ranged from less than 4 (three children) to 64 in the (V) group and 32 to 1,024 or greater in the (N) group.

Results.—In this and in all of our subsequent trials to date in which the L Sc strain of type 1 poliovirus has been used, none of the children has shown signs of illness such as those associated with mild or severe poliovirus infections. The induced infections were all inapparent and their existence was established by detecting poliovirus excretion over an appropriate time period, together with significant associated antibody rises.

There was a striking difference in the ease with which members of the V group (Salk vaccine immune) were infected with this large dose in this trial, as compared to the difficulty encountered in

infecting, or, more accurately stated, in reinfecting members of the N group. Thus in the first trial, in spite of the fact that some individuals had fairly high levels of antibodies against type 1 poliovirus, all 10 (100%) of the V group who were fed the

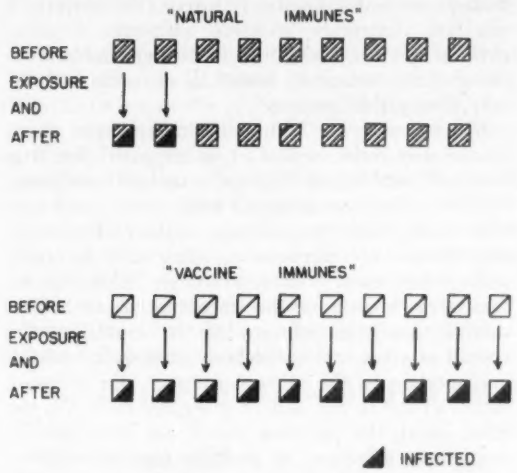

Fig. 1.—Diagram indicating number of infections after ingestion of attenuated type 1 poliovirus vaccine in first trial.

L Sc strain became infected; whereas only two of nine individuals in the N group (22%) became infected (fig. 1).

Bypassing the Pharynx.—It was possible to compare the effect of different methods of virus administration, whether by capsule or in liquid form, only in the vaccine-immune group, because so few of the children naturally immune became infected. Of the three vaccinees who received virus in capsule form, none excreted it subsequently in the throat, although all three excreted it in the feces. Of the seven individuals given the virus in liquid form, six had positive throat swabs, and all seven excreted virus in the stools. Absence of virus in the throat did not delay its appearance in the stool, nor was there any significant difference in antibody response in subjects with positive and negative swabs of the throat. These results confirm those of Koprowski and associates [1] and indicate that infection of the throat can be bypassed by feeding virus in capsules.

Spread of Infection to Contacts.—The spread of infection to their 49 associates from the 13 individuals who had been fed virus and who became infected was considerable. A diagrammatic illustration of what happened in the cottage appears in figure 2. Here, the upper panel illustrates the immune status of the 49 contacts occupying north and south wings at the time the 20 test children were fed virus. The north wing was occupied by somewhat older residents, aged 7 to 18 years (1 was aged 24 years), and the south wing by children aged 4 to 14 years. The lower panel illustrates the number of persons who became infected, both those who had been fed virus and their contacts. In all, the contacts numbered 49; among the 36 naturally immune (N), only 1 (3%) became infected, while among the 13 vaccine-immune (V) contacts, 12 became infected, or 92%.

This high rate of spread among the vaccine-immune children was understandably greater than that observed in an earlier trial carried out in the same institution, with attenuated type 3 poliovirus in adults within a hospital ward.[11] In the type 3 trial the subjects were older, probably more solidly immune, and the degree of intramural exposure was not so intimate. The amount of spread in the present study was also considerably greater than Sabin found in his early experience with type 1 strains in small groups of adults [2] and greater than Koprowski and co-workers reported among retarded children in an institution.[1] However, our present results are similar to those described by Dane and associates [6a] who fed Koprowski's SM strain of type 1 poliovirus to volunteers in Northern Ireland and found that this virus spread rapidly in a family setting. The influence of host resistance and of environment in conditioning the dissemination of the infection is obvious.

Actually, the speed with which attenuated poliovirus multiplied in the intestinal tract of the virus-fed children and the rapid spread within the cottage are important when considered in terms of

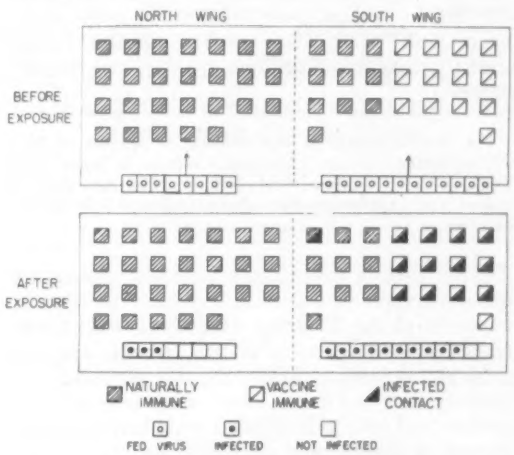

Fig. 2.—Intrainstitutional spread of infection of type 1 L Sc poliovirus vaccine in first trial.

the usual concepts of the length of the incubation period in natural human poliomyelitis infection. Of the 12 individuals who became infected (10 V and 2 N) 10 were already excreting significant quantities of virus by 24 to 48 hours after being fed, and the remaining 2 had positive stools beginning on the third day. Furthermore, seven days after the

test individuals had been fed, a number of contacts were also found to be excreting virus in their stools. This points to a one-day to three-day incubation period in terms of the establishment of an alimentary infection, and within a total of seven days or less at least two human passages had occurred. These observations confirm those of Dane and associates [6a] and earlier estimates by others of the shortness of the incubation period in poliovirus infection, which is considerably shorter than the usual textbook estimates of 9 to 12 days. The latter figure may apply for central nervous system symptoms, but by the time these appear the alimentary infection and excretion of virus have probably been going on for a week or more.

In addition to differences in susceptibility to the acquisition of intestinal infections, the individual patterns of virus excretion and antibody responses in members of the two groups (V and N) also differed: those with naturally acquired antibody had a much lighter infection, minimal virus excretion,

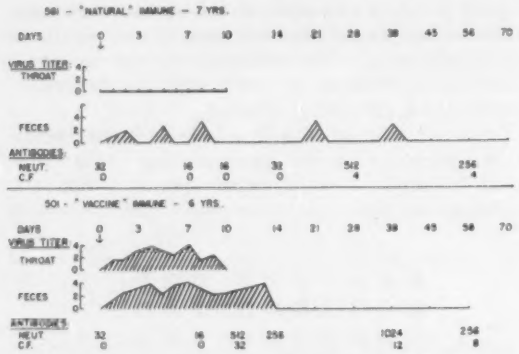

Fig. 3.—Responses in two subjects to feeding of $10^{7.4}$ TCD_{50} attenuated type 1 poliovirus vaccine in liquid form. *Top*, naturally immune child. *Bottom*, child who had acquired type 1 antibodies after administration of Salk (killed) vaccine.

delayed rises in neutralizing antibody, and no significant complement-fixation responses. In contrast, members of the V group, even those with appreciable prefeeding levels of Salk vaccine–acquired antibody, developed more extensive alimentary infections, excreted more virus, often over a longer period, and promptly showed complement-fixation as well as neutralizing antibody rises.

Samples of these two patterns of response are shown in figure 3. The naturally immune child (upper panel), aged 7, with a prefeeding type 1 antibody level of 1:32, became infected as evidenced by a rise in neutralizing antibody, but no virus was detected in the throat and excretion was intermittent in the stools. There was no significant complement-fixation antibody rise. In contrast was the response of a vaccine-immune child, aged 6 years, whose prefeeding type 1 antibody level, acquired from Salk vaccine, was also 1:32. This child excreted virus from the throat for 9 days, and considerable amounts were present in the stools continuously over a 14-day period. There was a sharp rise in both neutralizing and complement-fixation antibodies by the 10th day. The pattern of this first alimentary infection with type 1 poliovirus in this child was thus indistinguishable from the pattern commonly found in unvaccinated, totally susceptible persons.[2]

In retrospect, the difference in the types of response was more or less to be expected, for it is now well established that, under natural conditions, children who have received Salk vaccine and may have fairly high neutralizing antibody levels are nevertheless not immune to alimentary infection with polioviruses.[12] Thus, although killed vaccine does seem to achieve the important result of preventing paralytic poliomyelitis by curtailing the spread of virus within the body, it does not inhibit implantation in the alimentary tract, nor multiplication in the throat and/or intestinal tract. On the other hand, the previous experience of a natural, inapparent infection, or perhaps repeated natural infections with homologous poliovirus, probably does induce a condition of more solid resistance in the body's first line of defense. Consequently, when an avirulent poliovirus is administered in liquid form and comes in contact with the "experienced" pharyngeal or intestinal surfaces, it is less apt to gain a foothold or to multiply so extensively. The exact place where the virus multiplies and the exact part which antibodies (whether homologous or heterologous) play in this picture of host resistance to the initial implantation of a virus, which precedes the alimentary infection, has not yet been adequately determined.

Second Trial—March, 1957

Reinfection with Attenuated Poliovirus.—A second and smaller trial was carried out in the same institutional population four months after the first had been started. Objectives were to determine the ease of homologous reinfection of persons recently infected with attenuated type 1 poliovirus and to consider again the possible role, or existence, of a kind of "local immunity." In the second trial, 11 individuals (6 V and 5 N), 8 of whom had been infected in the first trial, were refed 16 weeks after their first exposure the same large dose, $10^{7.4}TCD_{50}$, of an aliquot of the same pool of L Sc strain of type 1 poliovirus. On this rechallenge, the number of persons who excreted virus in their stools was surprisingly large: all 11 individuals had at least one positive specimen, but in all excretion was briefer and more intermittent than on the initial feeding. Neutralizing antibody rises to a level above the relatively high prechallenge level occurred in only 3 of the 11 persons. Sample results illustrating some of the differences in the patterns of virus excretion

and virus infection are indicated in figures 4 and 5. In these two diagrams the responses of an original Salk-vaccine immune subject and of an original naturally immune subject are compared. The results of the first virus feedings (upper panels) and the rechallenge four months later (lower panels) are both shown.

The vaccine-immune child (fig. 4), on first ingestion of virus in liquid form, became infected, excreted virus in the pharynx and feces, and developed sharp neutralizing and complement-fixation antibody rises. On rechallenge with the same large virus dose in liquid form 16 weeks later, he failed to excrete virus from the pharynx, but stool specimens were positive intermittently through the 28th day. However, despite considerable fecal virus excretion, no rise in neutralizing antibody occurred, and the complement-fixation antibody rise was slight. This might be regarded as a superficial or limited alimentary infection.

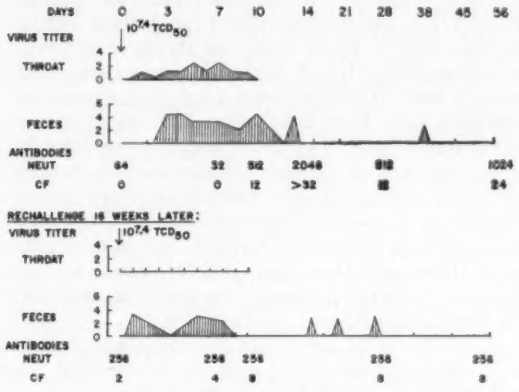

Fig. 4.—Response in 9-year-old vaccinated boy fed same large dose of attenuated type 1 poliovirus vaccine in liquid form on two occasions.

In comparison are the responses of the child from the N group, shown in figure 5. On first virus administration (in capsule form) no virus was detected in the throat, but there was minimal fecal excretion and a significant rise in neutralizing antibody. On rechallenge (lower panel) with the same dose, this time in liquid form, this subject again did not excrete virus from the pharynx, but did have several positive stool specimens as long as 28 days after virus ingestion, suggesting that reinfection occurred, although there was no rise in the already high neutralizing antibody level.

Results in relation to infection of the pharynx in persons in whom throat specimens were previously negative (or positive) are shown in the table. Two of three persons, who were initially Salk vaccinees and whose previous attenuated virus exposure and resulting alimentary infection had bypassed the pharynx by ingestion of virus in capsules, did excrete virus in the throat when rechallenged with the same dose in liquid form. In contrast, three naturally immune children, whose initial virus feeding also had been by capsule but whose throats had presumably already been exposed to virus naturally, i. e., some time before the first trial, resisted throat infection when rechallenged with

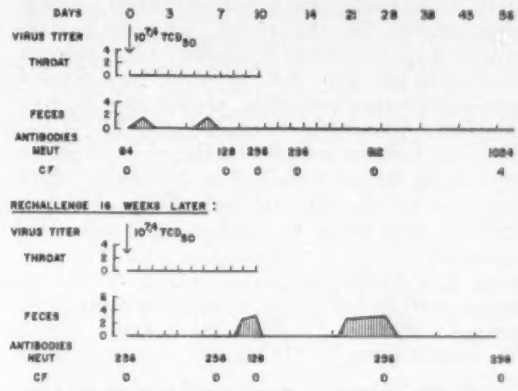

Fig. 5.—Response in 9-year-old boy naturally immune prior to being fed same large dose of attenuated type 1 poliovirus vaccine on two occasions—first in capsular form and later in liquid form.

attenuated virus given in liquid form. As listed in the lower part of the table, two of the three Salk vaccinees who were fed virus in liquid form on their initial exposure excreted it both in their throats and in their feces; on rechallenge, the feces were again positive but there was no evidence of throat infection. These data again suggest, although the numbers are small, that some type of "local immunity," due to a previous infection or infections, played a role in resisting the local, pharyngeal infection.

Relation of Virus Excretion from Throat to Mode of Administration and Previous Infection

No.	Immune Status	First Virus Feeding* Virus Excretion		Second Virus Feeding* Virus Excretion	
		Throat	Stool	Throat	Stool
		Capsule		Liquid	
526	V	−	+	+	+
540	V	−	+	+	+
513	V	−	+	−	+
553	N	−	+	−	+
571	N	−	+	−	+
583	N	−	−	−	+
		Liquid		Liquid	
503	V	+	+	−	+
514	V	+	+	−	+
527	V	−	+	−	+
504	N	−	−	−	+
570	N	−	−	−	+

* Virus dose $10^{7.4}$ TCD$_{50}$ L Se type 1.

Third Trial—November, 1957

Size of Dose in Relation to Capacity to Reinfect.—The ease with which reinfection with a large dose of virus was accomplished in the second trial

was somewhat disconcerting, but it prompted us to test the role of dosage in reinfection of the alimentary tract. It seemed that the large, almost massive dose used in the first two trials might occasionally have overwhelmed otherwise adequate levels of resistance. To test this the third virus feeding was started one year after the first trial and eight months after the second. The same 11 individuals from the second trial, and 5 other subjects ranging in age from 6 to 16 years, were divided into four groups and challenged with four different doses of virus ranging downward from $10^{7.4}TCD_{50}$ (figure 6). In these test subjects the prefeeding antibody levels ranged from 1:32 to 1:1,024 and there were low (32 to 128) and high (512 and higher) levels in each group. In addition, each group was composed of two V subjects who were originally, i. e., prior to the first virus feeding, vaccine-immune, and two N subjects who were originally naturally immune. As illustrated in figure 6, with the largest dose, $10^{7.4}TCD_{50}$, all four individuals

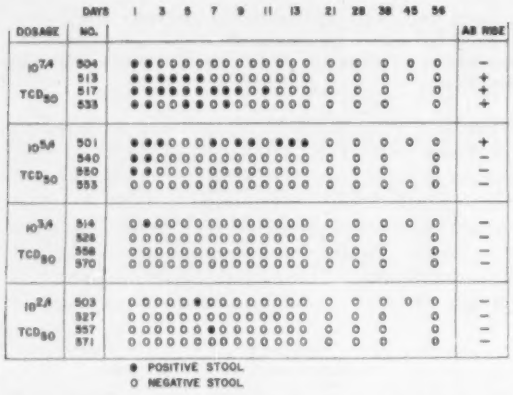

Fig. 6.—Response of 16 previously infected children to feeding of four different graded doses of L Sc type 1 attenuated poliovirus vaccine.

again excreted attenuated poliovirus in their stools, some of them for the third time, for periods ranging from 2 to 11 days. With a slightly lower dose, $10^{5.4}TCD_{50}$, one of the four subjects excreted virus for a period of 14 days, two individuals for only 2 days, and one individual failed to excrete virus at all. With the lower dosages, three of eight subjects excreted a single virus-positive stool. Only in four persons who received the larger dosages and excreted significant amounts of virus did rises in neutralizing and complement-fixing antibodies occur. These data are indicative of the fact that virus dosage is indeed important in initiating reinfection.

Stability of Attenuated L Sc Type 1 Virus

The important question of whether passage of attenuated virus through the human alimentary tract or its multiplication in some of the deeper tissues of the human body might alter its virulence was approached by comparing the neurotropic capacity of the virus fed with that excreted by infected persons. Tests were carried out by intracerebral inoculation of monkeys (rhesus and cynomolgus) with doses ranging from $10^{5.0}$ to $10^{7.4}$ TCD_{50}. The last positive stool specimens from 25 individuals were tested in a minimum of two monkeys in each instance. The material tested represented second tissue culture passage of the excreted virus, grown in the presence of a low concentration of bicarbonate, so as to favor multiplication of virulent particles should such be present.[13]

While the results indicate no striking differences between fed and excreted polioviruses in terms of paralytogenic capacity in monkeys, there was a slight increase in virulence of the excreted virus. The virus fed produced lesions and paralysis in only 1 of 14 monkeys (7%). Each of the 25 strains, representing isolation from 25 persons, was tested in two or more monkeys by the intracerebral route, giving a total of 67 monkeys; the result was paralysis in 5 (7%) and lesions without paralysis in 5 more animals (15%). In all instances the muscle weakness was minimal, and the lesions were sparse and usually mild. The specimens producing disease in monkeys were from 7 individuals of the 25 whose stools were tested. No signs or lesions were noted in more than half the animals inoculated, even though up to 25 million tissue culture doses were placed directly in the central nervous system. There was no significant difference between first human passage (from individuals fed) and the second human passage (infected contacts), in terms of excretion of more virulent virus by the latter.

A similar mild degree of reversion on passage in certain persons has also been observed by Sabin.[2] The virus used for feeding in our trials was purified by the terminal dilution method; although the gain in neurotropism was slight, it might well have been less had plaque-purified polioviruses of this same L Sc strain such as is now available [2] been used.

Comment

The trials described offered an opportunity to determine what actually happens when one starts an "immunizing epidemic" in a community of the kind under study. The first feature for emphasis is the demonstration that attenuated poliovirus infections can spread readily in a closed population where contact is intimate and there are enough susceptible persons present. Indeed, the spread is similar to that observed among susceptible children within a family when virulent polioviruses have been introduced inadvertently.[14] Furthermore, one relearns from the results that human immunity to poliovirus is not an all-or-none phenomenon and that it deserves quantitative rather than qualitative measurements. Correspondingly, the capacity of the virus to infect has a quantitative value, i. e., dosage.

Another feature which needs further exploration is the role of circulating antibody against polioviruses as compared with an as yet poorly defined defense mechanism which we have termed local resistance, or local immunity. In the three trials above described, it is clear that, as Fox and his colleagues have found,[12b] reinfection occurs in the presence of significant neutralizing antibody levels. There is evidence that adequate neutralizing antibody levels are a measure or at least an expression of something that limits the spread of poliovirus within the body, thereby preventing significant invasion of the central nervous system, but there is less evidence that such antibodies measure the strength of the barrier against implantation of the virus in or on the intestinal tract. In our trials, persons who had antibodies derived from vaccination with Salk vaccine became infected as readily as if they had had no experience with either live or killed poliovirus before. In contrast, however, persons with naturally acquired antibody of comparable level, who obviously had had previous local or topical experience with the virus, resisted intestinal infection to a greater degree, and when such infection occurred it was minimal. The same phenomenon was demonstrable in a few observations on throat infection of some of the children, as illustrated by the "bypassing" trials with the virus in capsules followed by challenge with virus in liquid form. These observations suggest that there exists some kind of tissue or, conceivably, humoral barriers in the alimentary tract—a hypothetical kind of resistance which we shall continue to term local immunity until a better name is suggested.

The number of persons on whom the trials have been conducted has been small. Uncontrolled and unknown variables have entered into the picture. However, with the kind of information obtained, one should be in a better position to observe and interpret findings of other field trials which deserve to be carried out in open communities with populations in different environments and with different degrees of immunity. Such trials are necessary if one is to learn more about the mechanism of infecting man in various environments with attenuated polioviruses, and the possible practical use of these agents in initiating, reinforcing, or maintaining immunity against poliomyelitis.

Summary and Conclusions

Sabin's L Sc live attenuated type 1 poliovirus was used within a small institutionalized population of juveniles. The capacity of the agent to infect and to reinfect members of this semi-immune population was measured in order to clarify the indications for the use of oral live attenuated virus vaccine as a means of initiating, reinforcing, or maintaining immunity against poliomyelitis. Children whose antibodies had been acquired from Salk vaccine were found to be infected readily, whether they were fed attenuated virus or exposed to infected individuals in the same cottage. In contrast, children whose antibodies had been acquired by previous natural infection were somewhat more resistant to infection in the same circumstances.

Our results indicate that a "local immunity phenomenon" can be demonstrated in the human alimentary tract; this is shown by the relative resistance of previously exposed persons to implantation of virus and alimentary infection. This kind of resistance seems to be closely related to a previous topical experience with poliovirus rather than to circulating antibody.

Virulence tests, with the L Sc strain used, were performed both before and after the virus had produced human alimentary infection. A slight increase in virulence was encountered under the latter circumstances, in that the virus isolated from the feces of some of the infected subjects showed a minimal increase in neurotropism for monkeys over that of the virus fed.

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PERSISTENCE OF ANTIBODIES AFTER VACCINATION WITH LIVING ATTENUATED POLIOVIRUS

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The duration of immunity produced by oral administration of living attenuated poliovirus has been investigated in three groups of children so treated since 1950. After the administration there was no apparent illness in any of the 26 subjects, but all developed antibodies and the virus was generally demonstrated in the feces. Tests for neutralizing antibodies showed that neither the young age of some of the infants nor their possession of transplacental antibodies had any discernible effect on antibody levels after vaccination and that the seven children in group A (who received the rodent adapted TN type 2 virus) all had type 2 antibody titers ranging from 1:16 to 1:256 approximately eight years after the vaccination. Vaccination with living attenuated poliovirus should theoretically induce lifelong immunity similar to that induced by the natural infection.

The prime requisite of a successful vaccine is the long duration of the immune state it produces. Natural infection by poliovirus apparently confers lifelong immunity as measured by serum neutralizing antibody.[1] Vaccination with living attenuated poliovirus should theoretically induce similar antibody persistence. This report consists of follow-up seroimmunological studies on some of the infants and children who have been fed attenuated polioviruses since 1950. The subjects included members of three trial groups: group A, children fed type 2 virus; group B, children fed type 1 virus; and group C, infants possessing transplacental antibodies fed types 1, 2, or 3 virus.

Materials and Methods

Group A.—The children in group A, all inmates of an institution, were among the first human subjects to be given attenuated virus by Koprowski

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and associates in 1950 and 1951.[2] They received the rodent-adapted TN type 2 virus, after which four of the seven children excreted fecal virus detectable in monkey kidney tissue culture. No attempt was made to isolate fecal virus by mouse inoculation.

TABLE 1.—*Persistence of Antibodies to Type 2 Poliovirus in Children Fed TN Strain—Clinical Trial Group A*

Subject*	Virus Dose Fed (Log_{10} MPD_{50})	Virus in Feces (Days After Feeding)	Reciprocal of Neutralizing Antibody Titer (No. of Mo. After Feeding Shown in Parentheses) 1-2 Mo.	33-72 Mo.	50-101 Mo.
2.....	5.0	4, 9	600(1)†	128(72)	128(101)
5.....	4.0	none	96(1)	16(72)	32(100)
7.....	2.1	13	256(1)	128(72)	64(94)
8.....	2.1	9, 13	256(2)	128(72)	64(91)
9.....	2.1	9	422(1)†	256(72)	128(94)
13.....	2.1	none	32(1)†	256(54)	16(94)
14.....	2.1	none	378(1)†	32(54)	16(94)
SC‡.....	5.5	11, 17	128(2)	256(33)	256(56)

* Original identifying numbers retained, as given in reference 2.
† Mouse protective test.
‡ Member of clinical trial group "B." (See text.)

Significant serum antibody titers obtained from these children three, four, five, and six years after vaccination have been reported.[3]

Group B.—Group B consisted of children in an institution who received the SM N-90 type 1 chick embryo–adapted strain of poliovirus in 1954 and 1955.[4] All subjects showed excretion of virus. Persistence of antibody has been reported at one year and at two and one-half years after vaccination.[5]

Group C.—Group C included normal infants less than 6 months old who were fed poliovirus in 1955-1957 by Koprowski and his colleagues.[6] The 13 infants each received one or two of four different vaccine strains: the TN type 2 strain, the SM type 1 strain, the monkey kidney–adapted CHAT type 1 strain, or the similarly adapted Fox type 3 strain. Fecal excretion of poliovirus occurred after all feedings with the exception of one with the TN virus.

Administration of Virus.—The virus was administered by bottle or dropper as virus-containing fluid diluted in milk or a similar bland vehicle. Detailed data relative to administration of virus and clinical observations were reported previously.[7]

Laboratory Studies.—The tests for neutralizing antibodies reported here were performed with monkey kidney or HeLa cells by either one of two methods: the metabolic inhibition test [8] or the roller tube test proposed by Gard.[9] The serums from groups A and B were titrated by the metabolic inhibition test. In all tests the 1958 serums were paired with serums obtained in 1955 or 1956.

Serums from Group C before and up to seven months after vaccination were also tested by the metabolic inhibition test, while serums obtained from this group in 1958 were tested by the Gard technique. Paired specimens from group C, with one exception, could not be tested, because serums obtained prior to 1958 were unavailable. The single earlier serum which was available gave a titer in the 1958 Gard tests identical to that observed previously with the metabolic inhibition test. Isolation of virus from stools was performed in monkey kidney tissue culture, according to a method already described.[10]

Results

All 27 subjects have remained well, without apparent illness as a result of their exposure to attenuated poliovirus. The determinations of neutralizing antibody in these subjects as well as pertinent data relative to their vaccinations are given in tables 1 to 3.

Group A.—Approximately eight years after vaccination, all seven individuals in group A have type 2 antibody titers ranging from 1:16 to 1:256, with a median of 1:64, as shown in table 1. The current titers on the average are one twofold dilution less than those demonstrated approximately six years after vaccination. In comparison with type 2 antibody levels determined one to two months after feeding, the current titers show a decline averaging about three twofold dilutions. Also included in table 1 and discussed below is a type 2 feeding to a member of clinical Group B.

Group B.—As shown in table 2, group B demonstrates the persistence of antibodies to type 1 attenuated virus for four and one-half years. The serums obtained in 1958 had titers ranging from 1:16 to 1:512, with a median of 1:128. These levels are below those determined approximately two and one-half years postvaccination by about one twofold dilution, but on the average are equal to those obtained one to three months after feeding. Subject SC, who was given SM type 1 and TN type 2 poliovirus simultaneously four and one-half years prior to the 1958 tests, retained antibodies to both types (tables 1 and 2).

TABLE 2.—*Persistence of Antibodies to Type 1 Poliovirus in Children Fed SM Strain—Clinical Trial Group B*

Subject	Virus Dose Fed (Log_{10} TCD_{50})	Virus in Feces (Days Inclusive After Feeding)	Reciprocal of Neutralizing Antibody Titer (No. of Mo. After Feeding Shown in Parentheses) 1-3 Mo.	27-34 Mo.	47-56 Mo.
SC	3.8	3-11	384(2)	512(33)	128(56)
JC	5.2	5-46	64(3)	512(34)	256(52)
Bo	4.2	3-51	384(1)	64(31)	32(50)
T	4.9	4-50*	96(1)	64(31)	16(50)
W	4.0	4-34*	128(1)	512(28)	256(48)
Ge	4.7	2-30	256(1)	1,024(28)	512(48)
Go	4.4	3-19*	32(1)	32(27)	64(47)

* Excretion not studied beyond this time.

Group C.—Fourteen feedings of attenuated poliovirus were given to the 13 infants in group C, as shown in table 3. Infant C2 was given separate feedings of SM and TN strains two months apart. The infants were vaccinated orally at 5 days to 6 months of age when moderate titers of transplacental serum antibody were present in all but one in-

stance. Such antibody apparently exerted no inhibitory effect on the active response to alimentary multiplication of poliovirus, except that antibody response to vaccination had to be judged not only by a fourfold increase in titer but also by the persistence of significant antibody levels beyond the time when transplacental antibody would be expected to survive. The method of judging the expected decline of such passive antibody has been described elsewhere.[6b]

The SM strain was ingested by seven infants, all of whom have maintained high levels of antibody (1:256 to 1:1,024) 15 to 28 months after feeding. The CHAT strain was administered to two infants, both of whom continued to have type 1 antibodies, approximately one year later. The TN type 2 strain was given to three infants, all of whom had antibodies 21 to 25 months after feeding. One of the three, however, retained a type 2 titer of only 1:6.

Two infants were bled 14 months after having received the type 3 Fox strain. While one of them (C37) retained type 3 antibody at a titer of >1:1,024, the other infant (C34) had no demonstrable antibody to type 3 virus even when undiluted serum was tested.

Infant C34 received $10^{5.5}$ TCD_{50} of Fox virus in December, 1956, when a titer of 1:64 of type 3 transplacental antibodies was present. Type 3 virus was isolated without difficulty from his feces on the 3rd, 7th, and 10th days postvaccination, but not on the 14th day. The type 3 antibody titer after feeding was 1:64 and 1:48 at 29 days and 56 days respectively. The titer thus remained stable for two months after vaccination instead of following the expected decline of passive antibodies. These data fulfill the criteria of a successful vaccination of infants as previously defined,[6b] but it must be noted that in the absence of definite evidence of an increase in antibody it is possible that in this subject a poor antigenic stimulus was produced originally.

Intestinal Resistance to Poliovirus Infection.—It was of obvious interest to determine whether intestinal resistance to poliovirus infection would remain after the loss of detectable antibodies in the serum of infant C34. Accordingly, 19 months after the original feeding in December, 1956, a second dose of $10^{5.5}$ TCD_{50} of Fox strain was given to infant C34. The results of the two feedings are compared in table 4. Type 3 virus was easily recovered from the stool after the first feeding by direct inoculation of a suspension into monkey kidney tissue culture, whereas after the second feeding similar direct inoculation of stool suspensions demonstrated only a trace of virus at 10 days after feeding. A blind passage of the tissue culture fluid from the tubes inoculated with stool suspension from this second feeding demonstrated type 3 virus on the 7th, 10th, and 14th days after feeding. The type 3 antibody titer, which was undetectable on the day of second feeding, rose to 1:64 one month later.

TABLE 3.—*Homotypic Antibodies to Poliovirus in Infants Fed Attenuated Strains of Virus—Clinical Trial Group C*

Strain	Type	Subject*	Age at Vaccination (Mo.)	Virus Dose Fed (Log_{10} TCD_{50}) †	Virus in Feces (Days Inclusive After Feeding)	Reciprocal of Neutralizing Antibody Titer to Type Fed (No. of Mo. After Feeding Shown in Parentheses)				
						At Time of Feeding	1 Mo.	2 Mo.	3-7 Mo.	11-27 Mo.
SM	1	C 2‡	3	4.7	1-56	64	64	712	1,024(3)	512(28)
TN	2		5	5.3	None	24	1,024		<128(5)	6(25)
SM	1	C 7	5	5.1	1-74	6	178	1,024		1,024(25)
SM	1	C 10	3	2.8	1-70	16	256	712		256(24)
SM	1	C 11	2	4.1	3-24	48	256			1,024(23)
SM	1	C 14	6	4.8	2-55	<4	362			1,024(20)
SM	1	C 26	5 Days	4.8	3-38	256	64	256	256(3)	512(20)
SM	1	C 32	2	5.8	3-52	96	64	1,024	712(3)	712(15)
CHAT	1	C 40	3	7.5	1-23	24	256			...§(12)
CHAT	1	C 46	1	7.5	1-26	48	64			128(11)
TN	2	C 6	5	5.3	Not tested	64	256		178(7)	>1,024(25)
TN	2	C 20	3	4.5	13-72	64	256	256	256(3)	256(21)
Fox	3	C 34	2½	5.5	3-10	64	64	48		0(14)
Fox	3	C 37	2	5.5	3-24	256	64	384		>1,024(14)

* Original identifying numbers retained, as given in reference 6.
† In TN feedings, 50% mouse paralytic dose.
‡ Infant C2 received both SM and TN.
§ Antibody detectable at 1:4, but serum not sufficient for titration.

Factors Related to Serologic Response.—In group C (table 3) neither the young age of the infants nor their possession of transplacental antibodies had any discernible effects on antibody levels after vaccination. For example, infant C26 was given the SM strain at 5 days of age when his type 1 titer was 1:256. He excreted poliovirus for 35 days after feeding and his type 1 titer rose to 1:256 at 3 months of age after an earlier drop to 1:64 at one month of age. Twenty months after vaccination a titer of 1:512 was present.

Natural Booster Infection.—The possibility was considered that booster infection by natural wild poliovirus may have contributed to the persistence of antibodies. In order to determine the likelihood of natural homotypic infection the heterotypic antibody titers (to poliomyelitis types not fed) were

studied in the most recent specimen from each subject. The results, presented in table 5, show that heterotypic antibody was absent in the majority of tests. In about 30% of tests, i. e., 33% for groups A and B and 24% for group C, such antibody had been acquired since vaccination.

TABLE 4.—*Response of Infant C 34 to Two Feedings of Fox Strain Virus Nineteen Months Apart**

Days After Feeding	Feeding 1—12/10/56 ($10^{6.5}$ TCD_{50}) Type 3 Fecal Virus	Feeding 1—12/10/56 ($10^{6.5}$ TCD_{50}) Type 3 Neutralizing Antibody	Feeding 2—7/15/58 ($10^{6.5}$ TCD_{50}) Type 3 Fecal Virus†	Feeding 2—7/15/58 ($10^{6.5}$ TCD_{50}) Type 3 Neutralizing Antibody
0	0	1:64	0	0‡
3	+	...	0(0)	...
7	+	...	0(tr.)	...
10	+	...	tr.(+)	...
14	0	...	0(+)	...
17	0	...	0(0)	...
21	0	...	0(0)	...
29	..	1:64	...	1:64
56	..	1:48	...	...
14 mo.	..	0‡	...	...

* Symbols: + = positive; 0 = negative; tr. = trace.
† Symbols in parentheses show results of blind passage.
‡ No type 3 antibody in undiluted serum.

Comment

The results in general support the concept that seroimmunity after live-virus vaccination is of long duration. The seven children in group A who were vaccinated with TN strain in 1950 or 1951 have been followed longer than any other recipients of poliomyelitis vaccine, either of living or inactivated virus origin. All have type 2 antibodies currently. The seven children in group B who were vaccinated with the SM type 1 strain four to four and one-half years before also retained antibody.

Group C is particularly interesting in that all but one of the 13 infants had transplacental antibody at the time of live virus feeding. Homotypic antibodies were present (table 3) one to two years after 13 of the 14 vaccinations in this group. One infant had lost all detectable type 3 antibody 14 months after feeding. This same child was demonstrated to have a relative "intestinal resistance" to type 3 poliovirus as judged by the low level of virus excretion which occurred after refeeding with Fox strain 19 months after its first administration (table 4). Resistance to intestinal reinfection has been demonstrated by Fox, Sabin, Koprowski, and Horstmann [11] in subjects immunized by both natural and attenuated polioviruses. In the case presented in this paper, intestinal resistance seemed to be independent of the presence of serum antibody.

It is possible that booster infection occurring in nature may have contributed to the maintenance of seroimmunity to the types fed in some of the children. The probability of homotypic natural infection was calculated to be roughly 30%, based on the percentage of tests for heterotypic poliomyelitis antibodies which were positive.

Another method of detecting natural infection is simply by retrospective analysis of antibody titers during the years after vaccination, some of which have been reported previously.[3] In four subjects, one in group A and three in group B, fourfold or greater increases in homotypic antibody titer have occurred since the original response to vaccination. Subject 8 in group A had an increase of type 2 titer from 1:24 at 54 months after vaccination to 1:362 at 71 months. In group B, the type 1 antibody of subjects SC, JC, and Ge changed at 9 to 15 months after vaccination from 1:16, 1:16, and 1:712, respectively, to 1:256, 1:1,024, and 1:4,096 on the next determination. The first of the two specimens from each child was obtained in May, 1955. The second serum specimen was taken in September, 1955, from two of the children (JC and Ge) and in December, 1956, from the third (SC). Since SC is a sibling of JC, and Ge lives in the same cottage, it is possible that a silent epidemic of type 1 poliomyelitis infection occurred in the institution during the summer of 1955.

Despite the question of natural booster infection, it is clear from these results that seroimmunity and intestinal immunity to poliovirus last for years after live-virus vaccination. The median duration of antibodies has yet to be determined but, on the basis of the present study, exceeds eight years. Intestinal resistance to poliovirus has been demonstrated in one case for at least 19 months after vaccination and may well be a more important criterion of immunity than the presence of circulating antibodies.

TABLE 5.—*Presence of Heterotypic Poliovirus Antibodies in 1958 Serums of Subjects Previously Given Attenuated Virus**

Group A Subject	Type 1	Type 2	Type 3	Group B Subject	Type 1	Type 2	Type 3	Group C Subject	Type 1	Type 2	Type 3
2	0	V	0	SC	V	V	+	C 2	V	V	0
5	+	V	+	JC	V	0	0	C 7	V	+	0
7	0	V	0	Bo	V	0	+	C 10	V	0	0
8	0	V	0	T	V	+	0	C 11	V	0	0
9	N	V	0	W	V	N	0	C 14	V	0	0
13	+ (trace)	V	0	Ge	V	0	0	C 26	V	0	0
14	N	V	+	Go	V	+	0	C 32	V	+	+
								C 40	V	0	0
								C 46	V	0	0
								C 6	+	V	0
								C 20	0	V	0
								C 34	+	0	V
								C 37	0	+	V
Totals											
V		7				8				14	
N		2				1				...	
+		4				4				6	
0		8				8				19	

* Symbols: 0 = antibody titer <1:4; + = antibody titer ≥1:4; N = natural antibodies before feeding; V = attenuated virus of this type previously administered.

Another method of detecting natural infection is simply by retrospective analysis of antibody titers during the years after vaccination, some of which have been reported previously.[3] In four subjects, one in group A and three in group B, fourfold or greater increases in homotypic antibody titer have occurred since the original response to vaccination. Subject 8 in group A had an increase of type 2 titer from 1:24 at 54 months after vaccination to 1:362 at 71 months. In group B, the type 1 antibody of subjects SC, JC, and Ge changed at 9 to 15 months after vaccination from 1:16, 1:16, and 1:712, respectively, to 1:256, 1:1,024, and 1:4,096 on the next determination. The first of the two specimens from each child was obtained in May, 1955. The second serum specimen was taken in September, 1955, from two of the children (JC and Ge) and in December, 1956, from the third (SC). Since SC is a sibling of JC, and Ge lives in the same cottage, it is possible that a silent epidemic of type 1 poliomyelitis infection occurred in the institution during the summer of 1955.

Despite the question of natural booster infection, it is clear from these results that seroimmunity and intestinal immunity to poliovirus last for years after live-virus vaccination. The median duration of antibodies has yet to be determined but, on the basis of the present study, exceeds eight years. Intestinal resistance to poliovirus has been demonstrated in one case for at least 19 months after vaccination and may well be a more important criterion of immunity than the presence of circulating antibodies.

In an isolated group of Eskimos studied by Paul and associates,[12] type 3 poliomyelitis antibodies were found only in those who were over 30 years of age. The data suggested that these antibodies had persisted approximately 35 years in the absence

of reinfection. This observation lends support to the theory that seroimmunity will persist indefinitely in most subjects infected with living virus and, coupled with the demonstration that vaccination can be successfully performed in early infancy, gives cause for optimism concerning the usefulness of living attenuated viruses as immunizing agents against poliomyelitis.

Summary

Type 2 poliomyelitis antibody was present in all of seven children approximately eight years after administration of the TN strain of living attenuated poliovirus. Type 1 poliomyelitis antibody was present in all of seven children approximately four years after administration of the SM strain of living attenuated poliovirus. Of 13 infants under 6 months of age at vaccination, 12 retained homotypic antibodies one to two years after feeding of the SM (type 1), CHAT (type 1), TN (type 2), or Fox (type 3) attenuated strains. The only child who no longer had demonstrable antibody to the type originally given was shown to be relatively insusceptible to intestinal reinfection by homotypic virus.

36th and Spruce streets (4) (Dr. Plotkin).

Barbara Cohen gave technical assistance for this study. Dr. Agnes Flack, Clinton State Farms, New Jersey, and Miss Dorothy Mooreby, New Jersey State Board of Child Welfare, assisted in making available the infants vaccinated in this study.

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TRANSPLANTATION OF BONE.—In recent years attention has been centered on transplants or grafts of osseous tissue, largely in connection with the healing of fractures or the filling in of defects in bone structure. There is now general agreement that transplants of fresh autogenous cancellous bone or of bone marrow may survive in the host bed and produce new bone. There is less evidence for the survival and growth of transplants of homogenous bone and little or none for the survival of heterogenous grafts. It is recognized, however, that implants of frozen-dried, devitalized, or preserved heterogenous bone may lead to production of new bone from the host bed, by induction. Similar results are reported for implants of the decalcified organic matter of bone and of bone mineral, prepared by removal of organic matter by solution in ethylene diamine.—Franklin C. McLean and Ann M. Budy, Connective and Supporting Tissues: Bone, *Annual Review of Physiology*, vol. 21, 1959.

SIMPLE CHEMICAL METHOD FOR THE DETERMINATION OF OVULATION TIME IN WOMEN

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The method here proposed for determining ovulation time requires that urine samples be collected nightly between 11 p. m. and 7 a. m. for from five to seven successive nights, beginning with the sixth or seventh day after midnight of the day the first menstrual bleeding occurs. The samples are tested by a special reagent for the presence of chemical substances as yet not fully identified; they give a blue color suitable for colorimetry. The color-yielding substance is a component of a complex containing a derivative of folic acid. Graphing the intensity of the color day by day yields a curve with a characteristic peak; the terminal low value, if it is on either the fifth or sixth day of the pattern, represents the day of ovulation. This hypothesis was tested by applying it to 227 cycles in which conception occurred by isolated coitus or husband or donor insemination. Among a total of 227 pregnancies there were 125 normal conceptions with full-term deliveries resulting from homologous or donor inseminations that afforded a basis for quantitative description of the ovulation pattern.

Various attempts have been made in the past to develop a simple, clinically applicable chemical method for the determination of ovulation time. None of these attempts has been found satisfactory. We report here a simple chemical procedure. The test, in its initial trial period, was compared with the Farris test (for hyperemia in the rat),[1] but no correlation was found. The new test has been applied independently of the rat test with gratifying results.

The test can be performed in any laboratory or medical office by a technician or nurse. One-tenth of a milliliter of daily urine is sufficient for a single test. The urine specimens of as many as 10 patients can be analyzed within an hour by an experienced person. The test has proved particularly useful in determining the ovulation time of patients with infertility problems. It is based on the measurement of the intensities of blue color developed in reactions between specific reagents and chemical entities produced in varying amounts by follicles and/or other organs believed to be stimulated or depressed by gonadotropic hormones during the ovulation cycle. Some information about the possible nature of the chemical entities responsible for the test results has already been obtained, but the discussion of their nature must wait for their final identification as the agents directly responsible for the results.

Procedure

Collection of Urine.—During the collection of urine for this test the patient should avoid drinking any kind of liquid—water, liquor, juices, or soda—and taking any kind of drug after 8 p. m. The urine voided between 8 p. m. and 11 p. m. should not be collected. The patient should collect all her urine nightly between 11 p. m. and 7 a. m. in individual clean, dry bottles and store it in a refrigerator after marking the date on each bottle. In this manner, urine is collected for from five to seven successive nights, beginning with the sixth or seventh day after midnight of the day the first menstrual bleeding occurred. From each of the collected urine specimens, about 1 fl. oz. (30 ml.) is transferred into individual clean, dry small bottles, stoppered or capped, and all the samples are brought on the last day for analysis. All the containers, large or small, should be labeled and noted with the name, date of collection, and cycle day. The bottles should be washed with distilled water (iron rust from faucets should be eliminated during washing).

Analysis of Urine Specimens.—Step 1: Before measurement bottles should be inverted several times for uniform dispersion of the contents. Measure 0.1 ml. of urine from each sample with an accurate micropipet of 0.1-or-0.2-ml. capacity into a correspondingly labeled standard or Klett-Summerson photoelectric colorimeter graduated for 5-and-10-ml. volumes. Care must be taken to wipe the excess urine from the tip of the pipet with a paper towel or filter paper. The pipet is then introduced to the bottom of the tube to prevent the loss of any trace of urine by contact with the inside of the tube. The pipet is rinsed with the urine of the succeeding sample before 0.1 ml. is measured for analysis, and so on down to the last sample in the series. This step is the most critical for the accuracy of measurements.

From the Department of Microbiology, School of Medicine, Wistar Institute of Anatomy and Biology, University of Pennsylvania, and Farris Institute for Parenthood.

Step 2: Add to each urine sample in succession 0.5 ml. from each of reagents 1, 2, and 3. Reagent 1 is a 10% solution of pure sodium carbonate; reagent 2 is a 0.1% solution of pure copper sulfate; and reagent 3 is known as Folin-Ciocalteu [2] reagent.

TABLE 1.—*Relation of Percentage of Four-to-Seven-Day Ovulation Cycle Patterns to Cycle Days During Which Conceptions Occurred, Based on 125 Conceptions*

Day of Conception	Patterns, % According to Length in Days				
	4	5	6	7	8
10	...	5.6	0.8	...	...
11	...	7.2	7.2	...	...
12	0.8	10.4	11.2	0.8	...
13	1.6	12.8	7.2	3.2	...
14	0.8	9.6	7.2	0.8	0.8
15	0.8	5.6	0.8	0.8	...
16	...	1.6	2.4	0.8	...
Total, %	4.0	52.8	36.8	6.4	0.8

These reagents can be measured with an ordinary graduated serologic pipet. Wait 10 minutes for the maximum development of blue color before diluting to the 10-ml. mark with distilled water, then mix the contents by inverting the tube with a clean thumb as stopper. Read the intensity of color in a Klett-Summerson colorimeter with filter 560.

Chemicals used for the preparation of reagent 3 must be of high purity. Into a 1.5-or-2-liter flask with ground glass joint introduce 100 Gm. of sodium tungstate ($Na_2WO_4 \cdot 2H_2O$), 25 Gm. of sodium molybdate ($Na_2MoO_4 \cdot 2H_2O$), 700 ml. of distilled water, 50 ml. of 85% orthophosphoric acid (H_3PO_4) solution, and 100 ml. of concentrated hydrochloric acid. After attaching a ground glass joint condenser reflux the contents gently for 10 hours. Then add 150 Gm. of lithium sulfate (Li_2SO_4), 50 ml. of distilled water, and a few drops of liquid bromine. Boil under a hood without condenser for 15 minutes to remove excess bromine. After cooling, dilute to 1 liter and filter through good quality paper into a thoroughly cleaned brown glass bottle or bottle adapted for plastic screw cap. The reagent should be stored in the dark and kept away from reducing agents. Before use, one part by volume of this reagent should be diluted with two parts of distilled water in a clean cylinder and stored for daily use in a glass-stoppered or screw-capped brown bottle.

Evaluation of Ovulation Time.—In the early period of experimentation an attempt was made to correlate the chemical findings with the day of ovulation determined by the Farris test. There was no direct correlation between the degree of hyperemia and the value of the chemical reading. A study of the fluctuating chemical levels revealed a rather uniform pattern. The chemical tests were then performed routinely. Once an adequate number of chemical studies were accumulated for cycles in which conceptions occurred the results were evaluated. It was observed that conception almost invariably occurred the fifth, sixth, or seventh day after the initial low point of the patterns. Considering the random nature of the chemical studies, it appeared significant that a conception rarely occurred on other days than these (table 1). Also, these patients were not forced into a formula which might allow conception by random chance; we are dealing with normal physiological variation as well as the human element in the urine collection.

These conceptions were achieved by isolated coitus, single insemination from husband, or single therapeutic insemination from donor. Primary weight was given to conceptions by therapeutic donor insemination with normally developing pregnancies or normal full-term deliveries. Of the 78 pregnancies used in the initial standardization of the chemical test 22 were in this category.

With the pattern established, the chemical test alone was applied to patients with established fertility problems in an attempt to achieve conception. Also, where the chemical tests were run parallel to the rat tests, if the rat test results appeared erratic or atypical the chemical tests were used as a guide for planned coitus or insemination. Further refinements of interpretation were added as the number of pregnancies accumulated.

Ovulation time was evaluated according to a pattern which is easily recognized by looking over the colorimetric readings of the urine samples from successive cycle days. This pattern extends principally over five or six cycle days. The pattern of the ovulation cycle begins with the lowest colorimetric reading, followed by a gradual rise to a peak, followed by an abrupt, gentle, or gradual drop in the colorimetric readings. This terminal low value, if it is on either the fifth or sixth day of the pattern, represents the day of ovulation. The pattern has the appearance of a triangle, the angle on the left side corresponding to the cycle day of the beginning of the pattern, the vertex to the cycle day of the peak of the pattern, and the angle on the right of the triangle to the cycle day of ovulation. Several representative examples from over 200 pregnancies are given in table 2.

Results

Chemical tests were performed during the cycle of ovulation in 227 cases. Of these 112 conceptions were achieved after the use of the chemical test alone for the selection of the attempt at conception, and 37 conceptions in cases where the rat test was performed but the day of conception was selected from the chemical studies, for a total of 149 conceptions. Of the 149 conceptions 33 were from single donor inseminations, with pregnancy either developing normally or having terminated normally. For these cases the average number of single donor inseminations resulting in conception was 2.02, with 18 (54.5%) occurring in the first month of treatment.

This compares favorably with the results achieved by other workers [3] relying on three donor inseminations on alternate days.

It should be pointed out that, from those who are eventually successful, the proportion of those who conceive in the first month is considered to be the most useful measure of insemination efficiency. In the group compared by Potter [3] the proportion of first-month pregnancies varied between 31 and 46% as against 54.5% in our series on the basis of a single insemination. Even in the most successful of the series reported by Potter, basal body temperature readings and occasional vaginal smears were employed. In this same group of 33 patients 6.1% conceived on the fourth day, 57.6% on the fifth day, 33.3% on the sixth day, and 3.0% on the seventh day from the initial low point of the chemical pattern. These values are comparable to the following percentages of conceptions: From 125 patients who conceived 4.0% had a four-day pattern length; 53.6%, five-day; 36.0%, six-day; and 6.4%, seven-day.

Two patients who required pelvic surgery for bilateral tubal obstruction had laparotomies in conjunction with the chemical test. In one patient, whose operation was performed on the predicted day of ovulation, a recently ruptured Graafian follicle was observed; in the other, whose operation was performed the day after the selected day of ovulation, a recently organized corpus haemorrhagicum was observed. The figure represents the chemical values for the same patient throughout the whole cycle from cycle day six for two consecutive cycles. In the first month (March, 1958) a single donor insemination was performed unsuccessfully. In the second month (April, 1958) the procedure was successful. The fluctuations in the chemical values in the two cycles are comparable to the higher values achieved in both instances during the preconception period. It should also be noted that the insemination was performed on the fourth day in the unsuccessful cycle, but on the corresponding fifth day in the successful cycle.

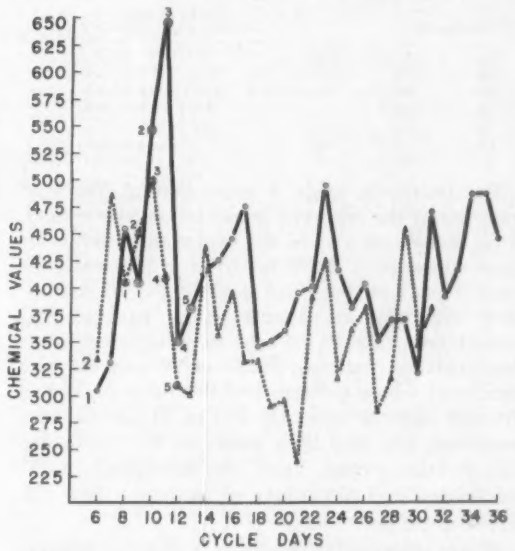
From the group total of 227 pregnancies 125 normal conceptions with full-term deliveries resulting from homologous and donor inseminations were used as a basis for the following calculations. Pregnancies due to coitus are not included for the reason that the exact day of coitus responsible for conception may be uncertain. The remaining pregnancies in the series were due to coitus or ended as miscarriages. Miscarriages are likewise excluded for the reason that it is not clear whether they are due to a too early or too late insemination or to the physiological condition of the subject or the ovum at the time of insemination.

As mentioned above, 53.6% of conceptions occurred according to the five-day pattern of the ovulation cycle and 36.0% according to the six-day pattern. That is, 89.6% of the conceptions occurred

TABLE 2.—*Representative Examples of Ovulation Cycle Patterns**

Cycle Day	Day of Pattern Peak 2nd	3rd	4th	5th
Typical Five-Day and Six-Day Patterns				
6.....	350	350	460	...
7.....	260†	460	290†	...
8.....	330‡	290†	340	...
9.....	290	340	360	...
10.....	260	360‡	400‡	...
11.....	200§	330	350	...
12.....	...	280§	270§	...
Examples of Acceptable but Less Uniform Patterns‖				
6.....	600	440	90	120
7.....	470	300†	80†	150
8.....	260†	320	180	120†
9.....	620‡	640‡	100	380
10.....	400	350	230‡	240
11.....	520	400§	120	480‡
12.....	400§	...	170§	540‡
13.....	...	...	...	240§

* Deviations = ± 25 from "normal" pattern. Consider height and range of values for individual pattern.
† Beginning of ovulation pattern.
‡ Peak days.
§ Ovulation day for insemination or coitus.
‖ Inseminations were on 5th and 6th day, in accordance with established patterns, even though 5th and 6th day values occasionally were slightly higher than ones immediately preceding. It is possible that more uniform and precise patterns might be obtained if, instead of single analyses of combined urine samples collected within period 11 p. m. to 7 a. m., various collections within each period were kept and analyzed separately. Use of such more elaborate procedure might result in obtaining sharper initial low points, pattern peaks, and last ovulation day within each pattern. Theoretically and clinically such a procedure might be desirable.



Chemical values for same patient throughout whole cycle from day six for two consecutive months. *Curve 1* (4/28/58), daily chemical values of month of conception: 1-5, ovulation cycle pattern; 5, day insemination (AID) was performed. Difference in chemical values between fourth and fifth days of pattern is not critical, particularly when values are of higher order. Perhaps critical lowest value could be obtained if hourly urines for fifth-day period were separately analyzed. *Curve 2* (3/2/58), daily chemical values for month conception failed: 1-5, ovulation cycle pattern; 4, day insemination (AID) was performed; 5, true day of ovulation on which insemination should have been performed.

according to five-day and six-day patterns. The remaining 10.4% occurred according to four-day and seven-day patterns. These are borderline patterns, and it may eventually be possible to group them with the others. These patterns are consistent with the known period of stimulation and maturation of the Graafian follicle. If the distribution of conceptions on cycle days is determined, it will be observed (table 1) that 79.2% of conceptions occurred on cycle days 11 to 15, according to five-day and six-day ovulation patterns.

TABLE 3.—*Interrelation of Number and Percentage of Conceptions to Percentage of Each of Pattern Peaks Within Each of Four-to-Seven-Day Ovulation Cycle Patterns, Based on 125 Conceptions*

Conceptions		Day of Peak	Patterns Peaks, % According to Length in Days				
No.	%		4	5	6	7	8
26	20.8	2	3.8	65.4	27.0	3.8	...
50	40.8	3	4.0	76.0	18.0	2.0	...
35	28.0	4	5.7	25.7	54.3	14.3	...
9	7.2	5	...	22.2	66.6	...	11
5	4.0	6	...	...	80.0	20.0	...

The results in table 3 show that in 89.6% of conceptions the observed peaks fell on the second, third, and fourth day of the ovulation patterns. Of these conceptions 40.8% occurred in patterns having the peak on the third day. Of the 26 conceptions occurring in patients whose patterns had second-day peaks, 65.4% were in patients with five-day ovulation patterns; 76.0% of 50 patients who conceived whose patterns had third-day peaks had five-day patterns; and only 25.7 of 35 patients who conceived who had their peaks on the fourth day had five-day cycles. From the standpoint of the mechanism and physiology of ovulation these differences are noteworthy.

If we analyze the results in a slightly different manner, we find (table 4) that ovulation patterns having their peaks on the second, third, and fourth day, respectively, show the occurrence of pregnancies predominantly during cycle days 11 through 14. In other words 84.6% of second-day peak pregnancies, 76.0% of third-day peak pregnancies, and 83.2% of fourth-day peak pregnancies occurred between cycle days 11 and 14.

The variation of peaks from the second to the fourth day brings out a new phenomenon which may mean either that certain follicular systems are more reactive to the stimulating agents or that the quantities of these agents are produced in different amounts in different ovulatory systems. The question of whether or not the relation of peaks to patterns varies from month to month in a given subject remains to be determined; however, in an individual patient in successive months the patterns are, in general, either consistently uniform or consistently irregular.

On the basis of the above-discussed results, the following considerations are evident: 1. Irrespective of the variation of the day, the peaks following the low point are the essential parts for the determination of the ovulation patterns and thereby the predicted day of ovulation. 2. Irrespective of the variation of the days on which the peaks were observed, 90% of conceptions occurred according to five-day and six-day long ovulation patterns. 3. Linked with 1 and 2 is the fact that 96.2% of conceptions occurred in patients with patterns having peaks on the second, third, and fourth days, on cycle days 10 to 15. Of these conceptions 50% occurred on cycle days 12 and 13.

Comment

The basic question in regard to the nature of the substances responsible for the results of the chemical test, particularly those underlying the occurrence of peaks during the ovulation cycle, cannot at present be answered. Preliminary tests show that the treatment of urine samples with weak acids and/or weak alkali with or without heating does not affect the test results. Chromatographic studies likewise show that none of the amino acids is responsible for the results. The presence of a certain class of substances collectively or individually responsible can, however, be conjectured. Of this class the flavonoids in urine need to be considered. They are biologically active substances which are invariably taken into the system in the form of seeds, vegetables, and fruits and are encountered in urine in their modified or original forms. A number of these substances have been estimated as to their potency for color development (table 5). What-

TABLE 4.—*Relation of Percentage of Pattern Peaks to Cycle Days During Which Conceptions Occurred (Based on 125 Conceptions)*

Cycle Day	Peaks, % on Day of Pattern				
	2nd	3rd	4th	5th	6th
10	7.7	8.0	5.7	...	...
11	15.4	14.0	8.3	33.3	...
12	34.6	20.0	22.8	33.3	40.0
13	15.4	24.0	31.4	11.1	...
14	19.2	18.0	20.7	11.1	40.0
15	7.7	10.0	5.7	11.1	...
16	...	6.0	5.7	...	20.0
No. of Conceptions	26	50	35	9	5

ever may be the nature of the urinary substances responsible for the color developed in 0.1 ml. of urine, during the ovulation cycle there is a definite increase in colorimetric readings which is responsible for the critical peaks in the chemical patterns.

The extraction from the thymus gland of a yellow substance with characteristics similar to the flavonoids has been reported, suggesting the possibility of the presence of flavonoids as components of the animal system.[4] In a symposium on flavonoids the following activities in the animal system were described[5]: Flavonoids inhibit succinoxidase via

the sulfhydryl group, choline acetylase, hyaluronidase, oxidation of ascorbic acid and epinephrine histidine decarboxylase, and release of histamine; they interact with different metabolites and enzyme systems linked with the regulation of capillary permeability by reducing fragility; and they act synergistically in the body with ascorbic acid. Other participants in this symposium reported that the flavonoid quercetin regulates the sexual process of the unicellular alga Chlamydomonas eugametos. l-Phenylalanine, 3,4-dihydroxyphenylalanine (dopa), meso-inositol, and 3,4-dihydroxycinnamic and 3,4-dihydroxyphenylpropionic acids function as precursors for the formation of quercetin. The naturally occurring isoflavonoids are estrogenic. In plasma vitamin C deficiency associated with decidual hemorrhage and spontaneous abortion a fruit diet rich in vitamin C and hesperidine has been stated to exercise a therapeutic effect, and a combination of vitamin C and flavonoids has been used in treating impaired capillary functions and capillary bleeding.

It has been reported that urine of 13 of 16 normal women showed the highest vitamin C level on the 12th to 18th days of the menstrual cycle, and the day of ovulation was denoted by an 80 to 100% decrease in the vitamin C content.[6] A relationship between the elimination of ascorbic acid in the urine and the basal temperature curve has been reported in a series of 32 women.[7] In 62.5% of the series the decrease in the excretion of vitamin C coincided with the characteristic drop in basal temperature. The menstrual period was characterized by poor elimination of vitamin C. In this connection it may be added that the lowering of ascorbic acid by norepinephrine is five times that by epinephrine.[8]

Epinephrine and a number of derivatives and precursors (table 5) are reported to be present in urine in appreciable amounts. 3-Methoxy-4-hydroxyphenylacetic acid[9] and 3-methoxy-4-hydroxy-D-mandelic acid[10] are major metabolites of norepinephrine and epinephrine. Dopa, dopamine, and 3,4-dihydroxyphenylpyruvic acid are reported to be the precursors of epinephrine.

In relation to ovulation time the interrelationship of platelets and epinephrine is noteworthy. It is reported[11] that the platelets consistently reached their highest levels during ovulation, as determined by basal body temperature graphs. In midcycle the levels of platelet counts usually rose suddenly and dramatically within 24 hours to reach the highest point during the entire cycle. Within another 24 hours the platelets returned to their previous levels and remained constant or decreased gradually until the onset of the next menstrual period. It was reported that the thermal shift coincided with that of the platelets. In view of the accepted facts that the basal temperature shift from the low to the high phase is indicative of ovulation and that ovulation may immediately precede or follow the temperature shift, Pepper[11] suggested that the platelet peak may be coincidental with ovulation in the vast majority of menstrual cycles.

Blood platelets are carriers of epinephrine and norepinephrine,[12] and they harbor 5-hydroxytryptamine.[13] It has also been reported that plasma epinephrine undergoes rapid and extensive changes in response to the injection of various hormones and drugs.[12] It was found that the injection of 20 units of ACTH daily for three days in four normal subjects resulted in a decrease in the excretion of norepinephrine but little or no change in excretion of epinephrine.[14]

TABLE 5.—*Colorimetric Values of Substances, Some of Which May Be Present in Urine*

Substance	Molecular Weight	Meg./Ml. Reaction System	Color Readings*
Miscellaneous			
Estrone (piperazine estrone sulfate) †	270.36	4.2	186
Thyroxin	798.90	1.8	252
Sodium Liothyronine	672.0	1.5	352
Serum albumin, crystalline	...	50.0	192
Ascorbic acid	176	4.0	239
Tyrosine	181.10	4.1	296
p-Hydroxyphenylpyruvic acid	180	4.0	330
Hydroxyproline	131.0	3.0	13
Flavonoids			
4-Methylesculin	192.00	1.0	202
3,4-Dihydroxychalcone	240.25	1.24	155
Genistein	260.00	1.24	150
Epicatechin	362.00	1.84	240
Quercetin	302.23	1.56	480
Naringin	580.33	2.90	88
3,3,4,4-Tetrahydroxychalcone	282.25	0.30	111
Hesperidin	610.55	3.20	170
Rutin	610.51	3.20	335
Hesperidin-methylchalcone	624.00	3.24	35
Phenyl and Indolalkylamines			
α-Indole-3-n-butyric acid	203.23	4.6	194
β-Indole-3-propionic acid	189.23	4.3	155
Indole-3-acetic acid	175.23	4.0	294
5-Hydroxy-Indole-3-acetic acid (Cyclohexamine Salt—mol. wt. 290.4)	191.23	1.32	208
5-Hydroxytryptophan	219.23	1.0	165
Tryptophan	204.11	4.6	106
5-Hydroxytryptamine (Creatinine Sulfate—mol. wt. 373.35)	162.00	0.74	141
Epinephrine	183.11	0.83	215
Parahydroxyphenylethylamine Hydrochloride (mol. wt. 173.56)	137.18	0.80	187
Tryptamine Hydrochloride (mol. wt. 197.00)	160.00	0.73	142
Dihydroxyphenylalanine (dopa)	197.00	0.90	240
Dopamine Hydrochloride (mol. wt. 189.54)	153.19	0.86	252

* Klett-Summerson colorimetric readings, filter no. 560.
† 5% sodium carbonate solution tested after 48 hours at room temperature.

A team of investigators[15] at the University of Edinburgh, measuring combined estrone, estradiol, and estriol excretion, reported finding a midcycle ovulatory peak in eight women with normal menstrual periods in whom the average total estrogen excretion was 56 mcg. per 24 hours. In view of the high colorigenicity (the property of a substance to yield a color in a reaction system) of epinephrine and related substances, and despite the low colorigenicity of estrone (table 5), the interaction of hormones and vitamins such as epinephrine, gonadotropic hormones, vitamin C, and flavonoids is evident.

Eventually it may be possible to correlate the sharp increases in urinary estrogen levels, the platelet peaks, and the known basal temperature shifts with the second, third, and fourth day peaks ob-

served by our chemical test in establishing ovulation cycle patterns for the further understanding of the physiology and chemistry of the ovulation cycle. Epinephrine and related substances may be responsible for the peaks we have observed and also may account for the platelet peaks and increases in estrogen output.

From the standpoint of characterizing the mechanism of the physiology of ovulation and reproduction we feel that we have a new simple tool to determine the nature of factors responsible for the chemical ovulation patterns. The following observations have recently been made: Folic acid derivatives present in 1 ml. of urine yielded a pattern paralleling the chemical ovulation pattern. Chlorides and para-aminobenzoic acid in these urine specimens have no correlation to the above patterns. Chromatograms of 0.1-ml. urine specimens show one main spot and at least two minor spots. In butanol–acetic acid–water solvent (50:25:25 by volume) the main spot has Rf value of 0.33, and one of the minor spots has Rf value of 0.86. The latter gives a positive ninhydrin reaction. In isopropanol–acetic acid–water (25:1:74 by volume) solvent the Rf of the main spot is 0.57. This substance has 284 mμ λ maximum and 254 mμ λ minimum. A similar compound is present in the male urine. The colorogenic main spots of both the male and female urine specimens have citrovorum factor activity. It would seem that the main spots are large molecules composed of a colorogenic substance, citrovorum factor, and possibly of other unknown substances. The hormonal, enzymatic, and chemical natures of these substances are being investigated.

We feel that the chemical ovulation patterns are completed with the beginnings of the chemical patterns corresponding to the ovulatory stimulation of follicles and the rupture of the Graafian follicles with the liberation of ova. Characterization of entities in the urine during this period would be expected to throw new light on the reproductive mechanism.

Summary

A simple chemical test based on color development, applied to first morning urine specimens for the prediction of the day of ovulation, was applied to 227 cycles in which conceptions occurred by isolated coitus or husband or donor insemination. In most instances a uniform, triangular five, six, or seven day pattern of chemical values afforded a basis for prediction of the day of conception. Of the 227 conceptions 149 were based solely on the chemical test predictions. Of patients who had single donor inseminations 54.5% conceived the first month of treatment. It took an average of 2.0 cycles for conceptions to be achieved in this group.

Thirty substances, hormones, vitamins, and chemicals, are analyzed by this test for their colorigenicity. Several of these may be factors responsible for the color developed in 0.1-ml. urine samples. Attention is called to the possible role of catecholamines and, particularly, epinephrine, norepinephrine, and related substances. There appears to be a close relationship among the peaks of platelet counts, estrogen output, and the colorimetric values which were observed in the present work, suggesting that in time a common causal factor may be found.

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George B. Koelle, M.D., Ph.D., Professor of Pharmacology and Dean of the Graduate School of Medicine, University of Pennsylvania, supplied many of the phenylalkylamines and indolalkylamines used in this study. Gustav J. Martin, Sc.D., Director of Research, National Drug Co. Research Laboratories, Philadelphia, contributed flavonoids; Abbott Laboratories, North Chicago, Ill., contributed the sample of piperazine estrone sulfate; and Smith, Kline & French Laboratories, Philadelphia, contributed the samples of thyroxin and sodium liothyronine.

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CRITICAL EVALUATION OF THE PSORALENS

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Opinions as to the usefulness of the psoralen group of drugs in treating vitiligo were obtained by questionnaire from 100 dermatologists in various parts of the world. Two dermatologists were enthusiastic about the systemic use of the psoralens, eight were vehement in their condemnation, and most considered the results poor. Systemic use of the psoralens caused a wide variety of disagreeable signs and symptoms such as nausea, vomiting, gastric burning, dermatitis, rectal bleeding, albuminuria, and jaundice. Animal experiments demonstrated eye damage (cataracts) and the development of tumors through probable photosensitizing factors. The psoralens are presumed to enhance tanning and increase resistance to sunburn. The use of drugs of such potential toxicity for what is primarily a cosmetic problem should be deplored. In those instances in which tanning is medically desirable, the results have been equivocal.

The Egyptians, since the 13th century, have been using for medical purposes the powdered fruit of the Ammi majus Linn, a plant found abundantly in the Nile Valley. Recently this plant has been identified as a member of the parsley family and is known in the United States as bishop's-weed, which grows in the western part of the country. Reputedly, use of these agents, the psoralens, resulted in pigmentation of vitiliginous skin, but side-reactions caused were nausea, vomiting, diarrhea, severe vesiculation, exfoliative dermatitis, and even coma. For a condition such as vitiligo, which was previously regarded as having no treatment of even minor helpfulness, such reports deserve investigation. Who knows but that from the ancient lore, whence came ephedrine, digitalis, and Rauwolfia, another drug may be emerging. The preparations, originally designated as ammoidin, ammidin, and majudin, were found to be identical, respectively, to the known compounds xanthotoxin, imperatorin, and bergapten [1] and are now designated as 8-methoxypsoralen, 8-isoamylenepsoralen, and 5-methoxypsoralen. The first of these is regarded as the most active,[2] the second is practically inactive, and the third is only moderately active photodynamically.[3] The generic name methoxsalen has been given to 8-methoxypsoralen.

The first scientific report on this subject, by el Mofty, appeared in the *Journal of the Royal Egyptian Medical Association* in 1948.[4] He republished his findings in English in the *British Journal of Dermatology*.[5] The psoralens were used orally, locally, and intradermally. A dose of ultraviolet light was given once or twice a week after the lesions were painted with solutions that were of varying concentrations. Response to treatment was noted in about three to six weeks and consisted of tiny hyperpigmented follicular spots and hyperpigmented growth from the edges. El Mofty stated that 5 of 15 patients were considered cured, 5 achieved a good response and 1 a partial response, and there were 4 failures. Five whose conditions were resistant to oral treatment showed response to intradermal therapy but none completely so. Of these, two showed response only after intradermal injections were supplemented by oral medication. Control areas treated with topical medication alone, ultraviolet light alone, or intradermal injections alone did not respond. Therefore, he concluded that results depend on a source of light changing the compound into a form which stimulates melanogenesis. Kanoff [6] subsequently confirmed this. Sidi,[7] in an attempt to evaluate intradermal therapy, found this mode of treatment very painful as well as ineffective in three of four patients.

Read at the McGuire Memorial Lecture Series, Medical College of Virginia, Richmond, Nov. 13, 1958.

Since the original report, many others have appeared. All the authors have used essentially the same over-all technique or attempted to evaluate one phase of the treatment. For example, some used varying doses of orally given medicaments, others varied the concentration of locally applied medicaments, and still others combined the local and systemic medication.

Although the classic approach to the discussion of a problem is a brief review of each article on the subject, I prefer to depart from this method and to discuss and, to some extent, evaluate the techniques used as reported in the literature. The discussion will be divided into evaluation of local treatment, systemic treatment, and combined treatment. In both local and systemic treatment, including "paired comparison," it is generally agreed that ultraviolet light (preferably sunlight) enhances the effect. The effective wave lengths appear to be between 2,500 A and 4,077 A.

Local Treatment

Those investigators using local treatment concerned themselves with varying the vehicle (cream or solution), the composition of the diluent, the concentration and composition of active ingredients, the frequency of application, the time interval between local applications of the medicament, and the use of subsequent irradiation. From this emerges a fairly standardized technique which consists of

first treating with a low concentration of the medicament (about 0.1%) and gradually increasing the concentration to tolerance point (usually not above 1%). The vehicle selected appears to make very little difference provided the active medicament is dissolved or uniformly suspended. The time interval of two to four hours between applications of the solution and the use of daily irradiation appears to give the best results. Some authors feel that the medicament should be washed off before ultraviolet irradiation is given, since the drug tends to filter out some of the rays. Exposure to ultraviolet light or sunlight must be as short as 5 to 10 seconds in the early stages of treatment and gradually increased in relation to tolerance, probably never much over 20 to 30 minutes. Uncontrolled sun exposure almost always results in severe reaction.

A limiting factor in the wide acceptance of this mode of therapy is a rather severe local toxic reaction which appears in practically all cases. This consists of swelling, blistering, oozing, and considerable associated pain, followed by marked scaling, pruritus, and hyperpigmentation. Occasionally, eczematization, ulceration, and even exfoliative dermatitis are also noted. Increased sensitivity to sunlight may persist for months without further application of 8-methoxypsoralen.[3] These reactions are often severe enough to incapacitate the patient completely for several days, particularly if the ultraviolet light dosage is uncontrolled.

Most authors agree that the degree of repigmentation is not dependent on the degree of reaction, since repigmentation has occurred with no reaction and has, at times, failed to appear after severe reaction. However, it is true that most patients who achieve repigmentation do so after severe reaction.

Systemic Treatment

The evaluation of systemic administration of the psoralens was concerned primarily with using varying percentages of the different psoralens and experimenting with varying doses. At present, the technique, after considerable trial and error, consists in administering 10 mg. orally three times daily or 20 mg. once daily. This is followed in two to four hours by daily use of ultraviolet light (sunlight if possible). Intervals of rest from the drug are advised by some. Again, most authors note that repigmentation is independent of the severity of the reaction. It is difficult to determine from the literature whether 8-methoxypsoralen alone is superior to combinations of drugs; certainly the effect is not statistically apparent. Sunlight exposure should be short, that is, 5 to 10 seconds at first with gradual increase to maximum tolerance. A protective cream should be used between ultraviolet exposures.

In the literature many [8] claim the superiority of local treatment over systemic therapy; others [9] report equally satisfactory results from systemic treatment alone. However, the marked reaction to be anticipated from local therapy eliminated to a large extent its wide acceptance except in use for small patches of vitiligo. At present the place of the psoralens in medical therapy largely depends on the effectiveness of systemic use combined with sunlight or ultraviolet light and on toxicity after systemic administration.

Evaluation of Treatment

Before evaluating any drug, one should know certain variables concerning the natural course of the disease for which it is used. Apparently there is no report concerning the frequency of spontaneous repigmentation in vitiligo, although I have noted it and it has been reported by others. I have also, on occasion, been able to note repigmentation after frequent local application of concentrated phenol to small patches of vitiligo or after the use of oil of bergamot followed by ultraviolet light, both procedures considerably less painful and less toxic than the use of 8-methoxypsoralen. It is not at this time evident whether there was a cause and effect in these procedures or whether spontaneous repigmentation occurred in these patients during the observational period of 8 to 15 months.

It is well known that hyperpigmentation often and depigmentation occasionally occur after a marked degree of inflammatory reaction in Negroes. Most authors using the psoralens noted that Negroes tend to respond more readily than Caucasians and children better than adults. Lesions of the face and trunk respond better than those of the mucous membrane, hands, and feet. Repigmentation practically never occurs in the genitalia. Lesions of recent origin respond better than those of long duration.

The over-all results obtained by authors varied so widely that evaluation is quite difficult. For example, in THE JOURNAL,[10] in November, 1955, is a statement that satisfactory results can be obtained in 30 to 40% of patients treated orally, 50 to 60% of those treated topically, and 80 to 95% of those treated by the combined methods. This observation was based on 200 recorded cases to date in the American and Egyptian literature. Sidi [7] reported significant repigmentation in 84% of 106 patients given oral treatment. Elliott,[11] in 1956, noted that 18 of 22 patients showed significant repigmentation by combined treatment and that the 4 who showed poor response had failed to cooperate properly. Levai [12] indicated that 54% of his patients who stated they had had previous skin trouble at the sites of their vitiligo and 68% without such difficulty achieved 95 to 100% repigmentation. Srivastava,[13] as well as Kelly,[14] indicated that 25% of their patients showed complete repigmentation, the former using combined and the latter local treatment. On the other hand, Sulzberger and Lerner,[15] in a recent article, reported that only 14% of patients achieved a satisfactory repigmentation, and Kanoff,[16] working on a large number of cases at the Skin and Cancer Hospital, as well as in his private practice, wrote that only 10% obtained a cosmetically acceptable repigmentation.

One must realize that the definition of satisfactory is relative, since some have regarded as satisfactory any repigmentation and others only significant repigmentation. Yet, from a cosmetic point of view, a small or even a significant amount of repigmentation often does not enhance the appearance. In my own series of 17 patients treated orally with doses of 10 mg. three times daily followed by weekly exposure to ultraviolet light, no patient achieved more than 50% repigmentation and, in most instances, less than this or nothing. Topical applications were abandoned after severe reaction in three patients without any significant response in any of them.

To evaluate this wide discrepancy in results, I sent a questionnaire to 125 dermatologists. A total of 100 replies were received from these men, who practiced in both small and large communities throughout the world; they varied from professors of medical schools to those with no academic connections at all. Twenty-four dermatologists did not use the drug for various reasons, mostly because they were afraid of the toxic effects. Only two dermatologists were enthusiastic about the systemic use of these compounds; one took them himself and gave them to his 4½-year-old daughter. Eight were vigorous in their condemnation of the use of these drugs, which they regarded as producers of serious reactions. Practically all others commented that their results were so poor as to show that while these psoralens might indicate an advance in the treatment of vitiligo they are certainly far from the answer. The breakdown in results is shown in the table.

Repigmentation After Use of the Psoralens

Method of Treatment	Cases, No.	Number Achieving Repigmentation				
		100%	75%	50%	25%	0%
Local	231	10	4	5	152	60
Systemic	999	31	6	286	338	338
Combined	113	0	0	17	55	41

It is rather interesting that all of the cases of complete or almost complete repigmentation were reported by 8 of 76 dermatologists who used the drug. All the rest reported 50% or less repigmentation in all their cases. In the present survey of the largest series reported to date, a really satisfactory result was obtained in 7.4% of 1,343 patients and in only 3% of 999 who were treated systemically. Admittedly there is a margin of error in a questionnaire type of report, but the large number of cases and the fairly consistent effects obtained by the majority of dermatologists perhaps reduce this error to statistical unimportance. Fitzpatrick, who is one of the leading authorities on pigment metabolism, reported at a recent meeting of the American Dermatologic Society that two to three years ago he had 150 to 200 patients under such treatment but during the past year only 4, a fact which would certainly indicate waning enthusiasm.

Sulzberger [15] stated that treatment response, even in the same individual, is erratic and that one course may give satisfactory results but on repetition may fail to do so. Treatment may have to be extended over a period of years. Many have commented that even during treatment new vitiliginous patches may appear and when therapy is discontinued the patient often relapses to the pretreatment status. When repigmentation occurs it often does so symmetrically.

Reactions

Immediate reactions reported with systemic use of the psoralens consist of nausea, vomiting, headache, gastric burning, excessive sweating, local redness, increased nervous tension, urticaria, oral and rectal bleeding, and albuminuria. Contraindications to systemic treatment are given as nephritis, hepatic insufficiency, diabetes, gastrointestinal abnormalities, hypertension, and cardiac disease.

During the early evaluation of these drugs, the investigators noted abnormalities in the cephalin flocculation and thymol turbidity liver function tests. However, Fitzpatrick,[17] in a later evaluation of these tests, felt that they were inadequate indicators of the potential liver damage caused by these drugs. He stated that the sulfobromophthalein test is the best indicator and, while he would hesitate to conclude that the drugs are safe for general use, he believed that the likelihood of hepatic damage has been overestimated.

Elwi [18] reported that animals who died of an overdose of 8-methoxypsoralen showed at autopsy pronounced changes in the adrenal glands, congestion and rupture of the sinusoids, total lipid exhaustion, degenerative changes of the liver, and some cloudy swelling and glomerular congestion of the kidneys. O'Neill and co-workers [19] noted that mice receiving intraperitoneal injections of 8-methoxypsoralen one hour prior to ultraviolet exposure exhibited severe erythema and an incidence of ear tumors of almost 100% as compared to 68% in a control group. Interestingly, the incidence of tumor development was less in the treated group than in the control group, to whom the drug was administered orally. Griffin and workers [20] have noted that with exposure to long-wave ultraviolet light, which is normally harmless, erythematogenic and carcinogenic effects were obtained with prolonged administration of the psoralens to white mice. Also, there was a high incidence (20%) of cataracts in the treated group but none in controls. They postulated that the slight long-wave ultraviolet emission from ordinary fluorescent lamps may possibly be sufficient to activate such changes if the animals are sensitized by the psoralens.

Rothman, in discussion, stated that if the long ultraviolet wave lengths (>3,650 A) which are emitted by sun and also by artificial fluorescent lights in offices acquire biological effectiveness through increased photosensitization and the potency of producing cancer and cataracts, dermatologists

should take a strong stand against their use. Fitzpatrick stated that the production of cancer under the experimental conditions used by Griffin has little application to the problem in man. He felt that conditions are not comparable, in that the dose given was far in excess of that used in man and the intensity and duration of long-wave ultraviolet light was of a degree quite impossible to obtain in sunlight. He further stated that he was unable to produce eye damage in albino guinea pigs by giving large doses of psoralens orally in conjunction with daily exposure to long-wave ultraviolet light over a period of nine months. Knox, however, pointed out that a man taking psoralens can be burned by the normally harmless Wood's light, as demonstrated by photographs of Stegmaier, and, consequently, that some of the findings in experimental animals are transferable to man. It would thus appear that final evaluation of the toxicity of this drug (which has to be taken over long periods of time and in repeated courses) is far from complete.

In the questionnaire two dermatologists reported jaundice within several weeks after oral administration of 8-methoxypsoralen had been started, and five reported abnormal liver function tests. Other unusual reactions noted were vertigo, pruritus vulvae, toughening of the nails, and appearance of eczematoid psoriasiform plaques only in areas of vitiligo. One dermatologist used 8-methoxypsoralen, with no undesirable effect, in two patients who had had hepatitis previously.

The mechanism of the action of the drug is unknown. Lerner states that there is no effect on the tyrosine pigment system unless possibly as sulfhydryl inhibition. Becker,[21] who studied histological changes in normal subjects who ingested 20 mg. of the drug daily followed by ultraviolet exposure, found that the most prominent change in the skin was a thickened, horny layer, resulting in an extremely compact layer and the formation of a stratum lucidum which is usually found only on the palms and soles. Becker feels that the natural exfoliation is thereby cut down and the pigment granules which normally are cast off are retained. The skin is thereby darkened and more responsive to ultraviolet stimulation. This type of change has been noted in the skin in general as a protective mechanism against solar dermatitis. Jarrett [22] noted that the melanocytes are present in the achromic patches of vitiligo but fail to be stimulated to produce melanin by ultraviolet light. Many other theories have been advanced concerning pathogenesis, but none has been experimentally proved.

Tanning Effects

During the course of the evaluation of the psoralens in vitiligo, another possible effect was reported—the ability to increase the tanning capacity of the skin. Lerner [23] noted that three of nine patients reported an increased tolerance to sunlight after oral administration of the drug. He then gave the drug to three albinos, who also believed that it conferred protection against the sun. Fitzpatrick [24] noted augmented tanning effect in patients taking up to 30 mg. per day two hours before sun exposure; but with doses over 30 mg. all the responses, that is, not only tanning but also erythema and blistering, tended to be augmented. Arnold [8a] believed that the chief value of the psoralens may well be their ability to facilitate suntanning and thereby to protect against sun-induced disabilities.

Daniel, Hopkins, and Fitzpatrick,[25] in an attempt to evaluate this possible tanning action, conducted a double-blind controlled study of burning and tanning effects in the summer. By random sampling one-quarter of their patients were given placebo, one-quarter active drugs, one-quarter placebo followed by active drugs, and one-quarter active drugs followed by placebo. A high percentage of patients were blue-eyed blondes. The 106 patients studied were unable to discriminate significantly between lactose placebo and 8-methoxypsoralen, as to both their sunburning and their tanning effects. Oddly, some examining physicians who did not know they had been giving placebo were enthusiastic about response. Here are a few comments from these physicians: "Tanner than ever," "Stayed out whole days without burning," "Increasing exposure and increasing drug dose without effect except more tan and no burn," and "wonderful." With masterful understatement, the authors conclude that perhaps the "testimonial" type of reporting has a high inherent error. Tanning effects apparently need to be studied by more objective criteria.

Since the toxic and photodynamic effects are as yet incompletely evaluated, it seems premature to use these drugs purely for cosmetic tanning. Certainly the statement of a pharmaceutical company that "thousands of physicians have employed these products for this purpose . . . without undesirable effects" is misleading.

Because of the reputed tanning effect, others have attempted to use the psoralens for conditions in which protection against the sun's rays is desirable—for example, in light-sensitive eruptions. No consistent results have been noted. In the questionnaire, good results were reported by one dermatologist in 3 of 5 cases of polymorphic light sensitivity and by three dermatologists in a total of 19 cases of various types of photosensitivity. It was used by 14 other dermatologists for a wide range of eruptions known to be aggravated by sun, with indifferent results. One noted a flare-up in a patient with polymorphic light sensitivity, and Elliott [11] reported two cases of this type of eruption in patients under treatment. Nine dermatologists reported on their use for the promotion of cosmetic tanning on an indefinite number of persons. Five stated that they felt there was a definite tanning effect; four felt that the patients were more impressed than they were. Many commented that they felt this drug should not be given for the tanning effect only since its safety is not completely evaluated.

Savitt [26] reported on its local use in alopecia areata and felt that the patch treated with the drug responded faster than comparable patches treated with phenol alcohol. Sidi [27] felt that favorable response was obtained by oral administration. Sulzberger wondered if a combination of the steroids and psoralens systemically might enhance the regrowth of hair in alopecia areata.

Conclusions

The toxic reactions in animals and the incomplete evaluation of toxic effects in humans certainly should strike a note of caution. Widespread and indiscriminate administration should be deplored and regarded as premature, since there are so many unanswered questions.

What will be the effect of increased sunlight exposure itself on increasing the incidence of carcinoma? Will the drug itself decrease or increase the development of skin cancers since both effects can be obtained by varied administration in animals? Will the "aging process of the skin" be accelerated or delayed? Will the increased melanogenesis activate junctional nevi or enhance the growth of melanomas? What are the harmful effects of long-term administration of these drugs on the gastrointestinal tract, liver, and kidneys and in humans with chronic disease or disability? How close to the 3% "cure" rate in vitiligo is the spontaneous cure rate? Do these drugs really increase tanning, and, if so, will those people who thereby expose themselves to sunlight be more subject to those afflictions to which excessive sun exposure makes them prone? Until these and undoubtedly other questions are answered, extreme caution should be exerted and the use of these drugs should be limited to experimental study.

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NOTE: A list of references may be obtained from the author on request.

ALTERED PROGNOSIS WITH CARDIAC MASSAGE

CARDIAC RESUSCITATION IN ACUTE MYOCARDIAL INFARCTION—REPORT OF TWO SUCCESSFULLY TREATED CASES

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and
Henry H. Gale, M.D., Detroit

In two instances patients with previous symptoms of myocardial infarction collapsed suddenly and became pulseless. Artificial respiration was given by insufflation, and immediate thoracotomy was performed to permit rhythmical manual compression of the heart, which was in a state of asystole. Intracardiac injection of 0.5 cc. of 1:1,000 aqueous solution of epinephrine was followed by ventricular fibrillation. Normal cardiac rhythm was restored by use of an electrical defibrillator in each case, and both patients survived without signs of injury to the brain. This is in accord with other published data indicating that these methods of resuscitation, if applied without delay, greatly improve the prognosis of patients with acute myocardial infarction.

The unusual occurrence of two successful cases of cardiac resuscitation outside the operating room in acute myocardial infarction within a three-week period at this hospital gave impetus to the present study of cardiac massage. The results of this investigation indicate that cardiac massage can alter the dire prognosis of patients with ventricular fibrillation or cardiac arrest complicating acute myocardial infarction.

With the number of recently reported cases of successful myocardial resuscitation in the last several years, cardiac massage has been thought of as a modern innovation. However, a review of the available literature indicates that the earliest attempt at cardiac massage occurred in 1874 [1] and the first successful resuscitation in 1902.[2] After this, there were other sporadic case reports of successful cardiac massage and defibrillation carried out in the operating room where surgeon, anesthetist, and equipment were immediately available. It was not

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until 1953 [3] that successful cardiac massage outside the operating suite was reported in the available literature. The present paper adds two more successful cases of cardiac resuscitation in acute myocardial infarction performed outside the operating room.

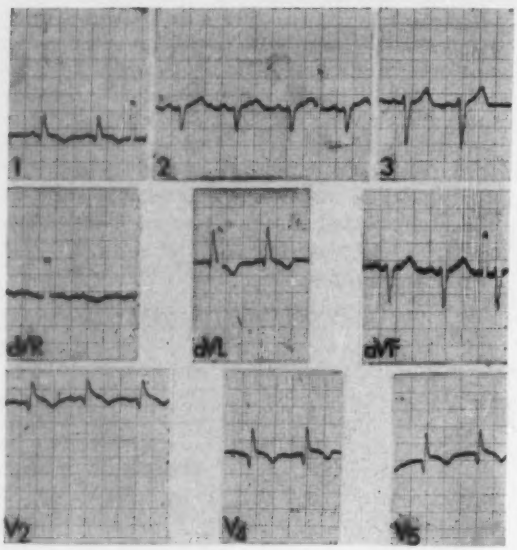

Fig. 1 (case 1).—Electrocardiogram taken two hours after cardiac massage, showing findings consistent with acute anterior myocardial infarction.

Report of Cases

Case 1.—A 53-year-old man was initially seen on Aug. 24, 1958, at the Henry Ford Hospital in the emergency room, where he registered with the chief complaint of left arm pain of several hours' duration. While removing his clothing in one of the examining booths, he collapsed to the floor. Both a surgical and a medical doctor in adjoining booths were able to reach him immediately. He lay on the floor in a tonic convulsion with contraction of masseter and extensor body muscles and with progressively increasing facial cyanosis. Rapid evaluation revealed the patient to be essentially dead without heartbeat, respiration, or reflexes. An airway was inserted, and intermittent positive-pressure breathing was initiated approximately one to two minutes after collapse. After the precordial area was pounded several times without results, an incision was made in the left fifth interspace. There was no bleeding from the skin and subcutaneous tissues, and the incision was extended into the thoracic cage. As rib retractors were applied, the lungs were seen to be expanding well. Cardiac massage, with use of the posterior approach and upward-palm-pressure technique, was begun by Dr. Emir A. Zikria and continued in teamwise fashion two to three minutes after collapse of the patient.

Initially no cardiac contraction was felt or seen through the pericardium, but after intracardiac injection of 0.5 cc. of a 1:1,000 aqueous solution of epinephrine, ventricular fibrillation occurred. The defibrillator was prepared, and 0.8 mg. of lanatoside C (Cedilanid) was injected into the heart for the purpose of strengthening the heart once fibrillation was stopped. Thirty minutes after initiation of cardiac massage, an alternating current was passed across the heart and apparent normal cardiac rhythm established. Bleeding became more active from the operative site, and the patient became very restless. He was taken to the operating room and his thoracotomy wound repaired. At this time, a small area of myocardial discoloration was noted on the anterior surface of the heart.

An electrocardiogram (fig. 1) taken in the recovery room immediately after surgical repair showed a normal sinus rhythm and changes compatible with an anterior myocardial infarction. A subsequent electrocardiogram (fig. 2) confirmed these findings. The patient was awake and alert eight hours after cardiac massage, with no evidence of brain damage. He told of having exertional left arm pain for four years; however, events of the day prior to his collapse were not recalled. Methoxamine (Vasoxyl) hydrochloride and levarterenol (Levophed) were needed for 48 hours to maintain the patient's blood pressure. There was no sign of oliguria, and his urinary output was excellent.

Laboratory studies the day of admission revealed a normal hemoglobin level. The white blood cell count was 19,000 per cubic millimeter. Urinalysis showed a specific gravity of

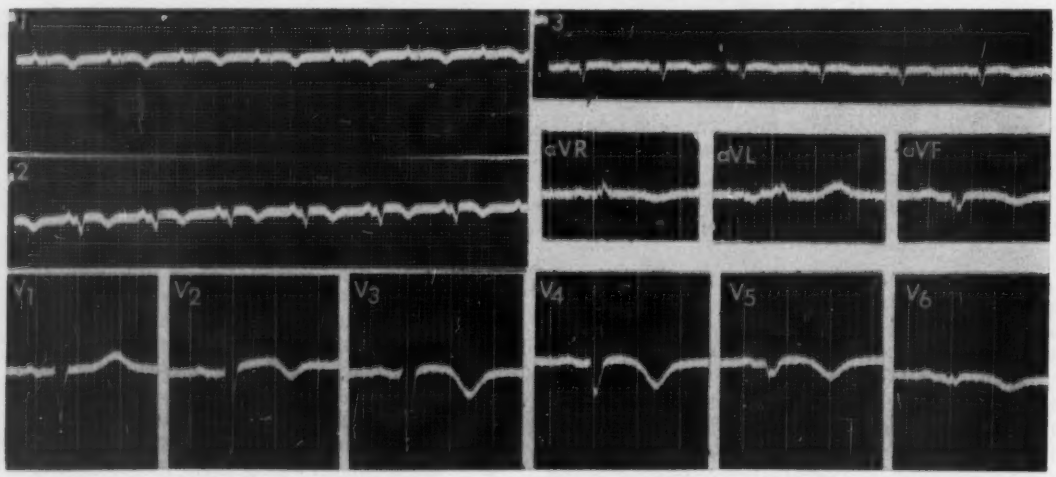

Fig. 2 (case 1).—Electrocardiogram taken four days after cardiac massage, confirming diagnosis of acute anterior myocardial infarction.

1.020, acid, albumin 4+, Benedict's test result negative, granular casts, many red blood cells, and 6 to 8 white blood cells. The urine cleared in seven days. The serum transaminase level was 150 units two days after admission; it decreased to 31 in 5 days and to 16 in 10 days. Initially chest x-rays were clear, but within four to five days a small collection of fluid was noted at the left base. The patient recovered uneventfully and is, at the time of writing (six months after admission), asymptomatic.

CASE 2.—A 40-year-old man was first seen in the outpatient clinic on Sept. 19, 1958, with the chief complaint of transient, burning retrosternal pain of four days' duration. The pain was present only with activity and radiated to the left shoulder and down the inner aspect of the left arm. A physical examination gave normal findings. The blood pressure was 140/90 mm. Hg and the pulse rate 72 per minute and regular. The initial impression was coronary artery insufficiency with impending myocardial infarction, and the patient was admitted to the inpatient service. The transaminase level determined at this time was 12 units, and an electrocardiogram showed, as the only abnormality, a slight ST-segment depression in leads V_5 through V_4. While the medical floor resident was making rounds the next morning, the patient's respirations suddenly ceased. He appeared cyanotic and lifeless, and no heartbeat was audible. Approximately three minutes after his collapse, a thoracotomy was performed by Dr. M. A. Block. Cardiac massage and mouth-to-mouth breathing was started, and an intravenous cut-down was placed in the patient's right leg. After about 0.5 cc. of a 1:1,000 aqueous solution of epinephrine was injected into the heart, weak ventricular fibrillation started. The patient was taken to the operating suite for defibrillation with the defibrillator and surgical repair 45 minutes after arrest. Levarterenol was used for 72 hours to maintain the patient's blood pressure. Urinary output was good. There was no suggestion of cerebral damage, and the patient talked rationally about eight hours later.

Laboratory studies obtained just after the cardiac arrest revealed a white blood cell count of 14,000 per cubic millimeter, hemoglobin level 12.6 Gm.%, and nonprotein nitrogen level 30 mg.%. Urinalysis revealed a specific gravity of 1.014, neutral, albumin 1+, Benedict's test result negative, few hyaline casts, 25 red blood cells, and 50 white blood cells. The transaminase level remained at 100 units for three days and then decreased to 60 units on the fourth day. Chest x-rays revealed a minimal amount of fluid in the left lung base. The patient was asymptomatic five months after his cardiac standstill. Electrocardiographic findings (figs. 3 and 4) had been consistent with an acute anteroseptal myocardial infarction.

The medical records of five cases of cardiac arrest in acute myocardial infarction with cardiac massage at this hospital were reviewed (see table).

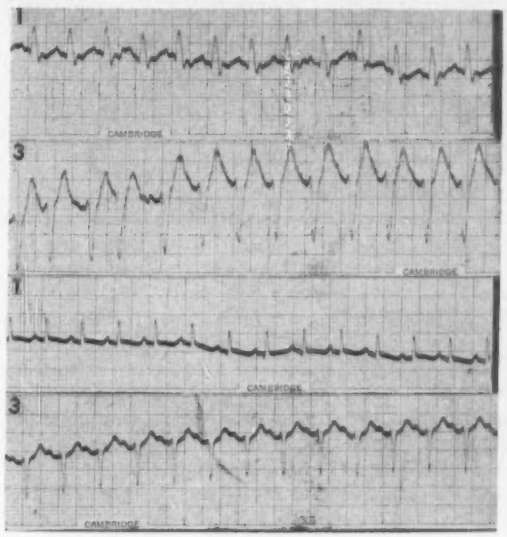

Fig. 3 (case 2).—Electrocardiogram taken *(top)* two and *(bottom)* five hours after cardiac massage.

In all of these cases, massage of the heart was performed either in the emergency room or in the patient's hospital room. Of these five patients, three presented the clinical picture of an impending myocardial infarction. Laboratory studies prior to cardiac arrest were available in two. Electrocardiograms showed ischemic changes, while the white blood cell count, sedimentation rate, and trans-

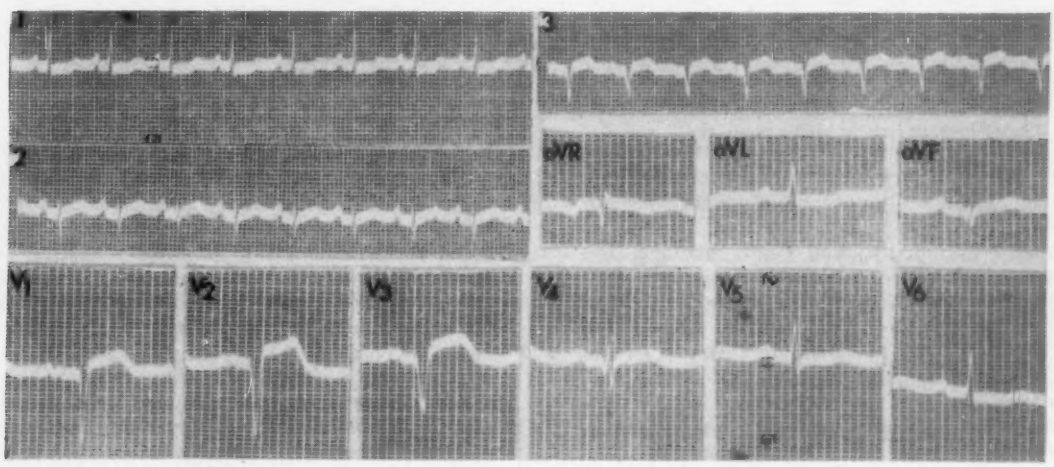

Fig. 4 (case 2).—Electrocardiogram taken three days after cardiac massage, showing findings consistent with acute anteroseptal myocardial infarction.

aminase level were normal. The fourth patient was treated for a pulmonary infarction and initially thought to have a normal cardiac status. The fifth patient was an elderly diabetic with severe chronic congestive heart failure, shown to have an old myocardial infarction at autopsy. At the time of cardiac arrest, a rapid examination was carried out on each patient. The examining physician noted a cadaveric appearance to the body in each case and was not able to detect any respirations, heartbeat, or reflex response. Cardiac resuscitation was carried out successfully in four of the five patients. However, two died shortly after massage. The cause of artificial respiration and nasally given oxygen did not provide enough air pressure to fill the lungs completely. Intracardiac administration of epinephrine was used in three cases, and ventricular fibrillation resulted. One patient also received intracardiac treatment with lanatoside C. Whether these drugs were beneficial or not is difficult to say. Levarterenol appeared necessary to maintain blood pressure in the patients who were rescued.

Autopsy material confirmed the clinical evidence of acute myocardial infarction in the three patients who died. A fresh thrombus was found in the left circumflex coronary artery of one, while throm-

Results of Cardiac Massage in Five Men with Acute Myocardial Infarction

	Case No.				
	1	2	3	4	5
Age, Yr.	53	40	38	50	60
History					
Previous myocardial infarction	None	None	None	None	Anteroseptal myocardial infarction
Previous heart disease	Slight transient angina, 4 yr.	None	None	None	"Arteriosclerotic heart disease," heart failure
Chief complaint	Episodic pain in left arm, 12 hr.	Impending infarction, 4 days	None	Impending infarction, 12 hr.	None
Location at arrest	Emergency room	Inpatient	Inpatient	Emergency room	Inpatient
Treatment after arrest					
Pulmonary ventilation	IPPB*	Mouth-to-mouth	Nasally given oxygen, artificial respiration	Nasally given oxygen, artificial respiration, IPPB* 20 min.	Mouth-to-mouth artificial respiration, not continuous
Duration of massage, min.	30	45	5 to start, 45 2nd time	20	20
Intracardiac drug therapy	0.5 cc. of 1:1,000 epinephrine, lanatoside C	0.5 cc. of 1:1,000 epinephrine	None	Epinephrine, nikethamine	Calcium chloride, isoproterenol
Defibrillator	Converted	Converted	Not used	Converted	Not used
Levarterenol	48 hr.	72 hr.	Not used	9 hr.	Not used
Chest pounding	No help	No help	No help	No help	No help
Results	Alive and well	Alive and well	Lived 10 min.	Lived 9 hr.	Died immediately
Electrocardiograms					
Before massage	None ↓	S-T segment depression V_2-V_4 "ischemia" 12 hr. ↓	Normal 1 wk. ↓	S-T segment depression V_2-V_6 normal transient "ischemia" 3 hr. ↓	Old anteroseptal infarction 2 days ↓
After massage	Acute anterior myocardial infarction	Acute anteroseptal myocardial infarction	...	Acute myocardial infarction	...
Consciousness regained and lucid, time	8 hr.	8 hr.	Never	Never	Never
Factor in failure	...	...	Overwhelming emboli	Poor pulmonary aid	Poor health of patient
Autopsy results	...	...	Multiple emboli to brain, lung, and right coronary artery	Fresh thrombosis in left circumflex coronary artery	Old anteroseptal infarction, fresh thrombus with posterolateral infarction

* IPPB = Intermittent positive-pressure breathing.

death in one of these patients was probably brain damage secondary to poor initial pulmonary ventilation. The other patient died from widespread embolic occlusion 10 minutes after massage. The unsuccessful case of cardiac resuscitation was in an elderly man with diabetes mellitus and severe congestive heart failure. Two patients, whose cases are reported above in detail, are alive and well at the time of writing and show no evidence of brain damage.

Adequate pulmonary ventilation was as important in the success of resuscitation as the actual cardiac massage and defibrillation. Intermittent positive-pressure breathing and the mouth-to-mouth method were both satisfactory to keep the patient breathing and his blood oxygenated. In contrast, bophlebitis with multiple fresh emboli to brain, lung, and right coronary artery was noted in another. The patient who died almost immediately after cardiac massage had, at autopsy, a fresh thrombus in the anterior descending branch of the left coronary artery and an old anteroseptal myocardial infarction.

Comment

Several theories have been advanced to explain the cause of sudden death in apparently normal persons and those with coronary artery disease. Many depend almost entirely on some type of neurogenic mechanism. White [4] suggested that excess reflex stimulation of the vagus nerve, with paralysis of the pacemakers or ventricular fibrilla-

tion, could cause sudden death. Beck and coworkers [5] postulated that death from coronary artery disease occurred in either one of two ways: The majority (90%) were due to electrical instability; the remainder (10%) were due to actual cardiac muscle failure. Oxygen differentials in contiguous areas of heart muscle, such as is produced by coronary artery insufficiency or myocardial infarction, produces electrical currents which are responsible for the arrhythmias that kill. It has been estimated that electrical instability without initial muscle damage kills one-third of all victims with acute myocardial infarction. In the other two-thirds, myocardial damage is present but not significant enough to prevent the heart from responding to cardiac massage. Since it has been estimated that sudden death due to cardiac disease occurs 10,000 times each year in the United States alone, the potential of cardiac resuscitation in patients with coronary artery disease who die because of arrhythmia is great. Four patients presented in the present series (see table) responded to cardiac massage with a normal cardiac rhythm. This would support Beck's theory that most cases of cardiac arrest are due to electrical instability and not secondary to irreparable myocardial damage. The one patient whose heart did not respond in any way to cardiac massage was in extremely poor physical condition.

Bloomfield and Mannick [6] feel that it is necessary to document the myocardial infarction prior to arrest to discern the necessity of thoracotomy. They also suggest that the electrocardiographic changes of myocardial infarction noted only after the cardiac massage in most cases reflect manipulative trauma rather than true myocardial infarction associated with coronary artery disease. In this study, all patients presented without evidence of acute myocardial infarction until cardiac arrest occurred. The acute myocardial infarction itself appeared to be the immediate, initiating event for cardiac arrest. To investigate the possibility that the electrocardiographic changes were on the basis of cardiac massage, the medical records of six living patients who developed cardiac arrest in the operating room, as a complication of operations, were reviewed. No heart disease was evident in any of these patients, and preoperative electrocardiograms were normal. After cardiac massage, no change or abnormality could be detected in repeated electrocardiograms. Cardiac manipulation or massage per se, therefore, would appear not to produce electrocardiographic changes of acute myocardial infarction. The acute myocardial infarction pattern that occurred in the two patients in whom cardiac resuscitation was successful was on the basis of true coronary artery disease. In fact, a damaged area was seen in the first patient during massage.

In the heart with ventricular fibrillation, cardiac massage is necessary as a preliminary measure to improve myocardial oxygenation and tone prior to attempts at electrical defibrillation, and also to prevent a recurrence of the fibrillation. Wiggers [7] demonstrated in dogs that ventricular fibrillation regularly occurred after ligation of a coronary artery. Defibrillation with electric shock was always possible, but fibrillation recurred unless the tie occluding the coronary vessel was removed and myocardial oxygenation improved. Four minutes has been set as the time limit within which adequate circulation must be artificially established.[8] In dogs, complete arrest of cerebral circulation for greater than three minutes and 25 seconds produces irreversible neurological changes.[9] In a review of cases collected from the entire United States, there was a much higher survival rate when the massage was started within four minutes, as contrasted to when it was started after this.

From observation of the two recent cases of successful cardiac resuscitation in acute myocardial infarction and from the analysis of three other cases with massage, an altered prognosis is at hand for many patients who would otherwise die from acute myocardial infarction. If a patient with good myocardial reserve develops myocardial infarction with arrest or ventricular fibrillation, cardiac massage may be a life-saving measure. Immediate restoration of effective circulation, as well as adequate ventilation, is vital.

Summary

In two patients with cardiac arrest in acute myocardial infarction, successful cardiac resuscitation occurred outside the operating room. There is, with cardiac massage, a favorable prognosis in cases of cardiac arrest or ventricular fibrillation in acute myocardial infarction.

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SOME NONTECHNICAL ASPECTS OF OPEN-HEART SURGERY IN THE COMMUNITY HOSPITAL

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Considering present world-wide birth rates and figures relative to the incidence of congenital heart disease, fewer children are given the opportunity for corrective surgery within a year with present facilities than are born eligible within a given day. This fact does not take into consideration surgical candidates with acquired heart disease. Open heart operations are feasible within hospitals at the community level. The equipment needed is not as complicated as so often anticipated, and the chances for success are good if the proper personnel equip themselves with certain unpurchasable principles and if confusing, complicating, and obstructing attitudes and gadgets are kept out of the operating room. Particular emphasis is placed on thorough indoctrination of the entire team in the laboratory. The necessary personnel can usually be found, and the equipment acquired, by smaller communities as well as by larger ones, leaving only certain intangible personal traits to decide success or failure.

Four years of endeavor in the experimental laboratory and operating rooms in community hospitals has afforded ample opportunity to face challenging issues which should be of interest to others embarking on a similar course. Eliminating the purely scientific and technical problems encountered in undertaking open-heart surgery with use of a pump oxygenator, the thesis can be broadened to encompass almost any major, unique, and "drastically new" scientific project at the same civic level of medical and surgical practice. These problems should be of special interest to all young men who wish to go beyond the fringe of established and readily acceptable medical practice.

The subject may be divided into the following headings: (1) the practicability of open-heart surgery in the community hospital; (2) the availability of case material; (3) assembling a team; (4) preliminary experimental experience; (5) preoperative evaluation and selection of patients; and (6) some perplexities encountered at the beginning.

Practicability of Open-Heart Surgery in the Community Hospital

Cardiac surgery with a bypass pump oxygenator has become an established procedure in an ever-increasing number of institutions. To be sure, numerous problems pertaining to details, especially regarding oxygenating mechanisms, remain, but these are rapidly diminishing. Ambition for use of the new operation has become almost irrepressibly contagious among thoracic surgeons throughout the United States, and the problems involved are diminishing through its constant success.

In some institutions, the mechanical heart is in daily use and hundreds of patients owe their survival to it. A survey of the waiting lists of patients referred to some of the more well-known centers indicates increasing acceptance by medical men throughout the world. An impressive listing of cardiovascular anomalies considered applicable to bypass extracorporeal techniques is as follows: Congenital anomalies include ventricular septal defects, single ventricle, atrial septal defects, atrioventricular canal, tricuspid atresia, downward displacement of the tricuspid valve (Ebstein's disease), anomalous pulmonary venous drainage, pulmonic valvular and infundibular stenosis, tetralogy of Fallot, transposition of the great vessels, aortic sinus aneurysm, anomalous coronary arteries, aorticopulmonary window (aortic septal defect), subaortic stenosis, aortic regurgitation, and endocardial fibroelastosis. Acquired anomalies include aortic stenosis, aortic regurgitation, mitral stenosis and regurgitation, rupture of the sinus of Valsalva, intracardiac tumors, thoracic aortic aneurysms, and rupture of the ventricular septum.

Those with the greatest experience have shown that the mortality resulting from the operative intervention in certain congenital anomalies of the heart (e. g., interventricular septal defect), uncomplicated by some additional defects, such as severe pulmonary hypertension, and the effects of time-consuming indecision and unwarranted procrastination, can fall well within the justifiable limits of 2 to 3%. Other lesions of a more complicated and hazardous nature have mortalities well below those for the medical treatments assigned them. A continued downward trend attends operative experience. Indeed, the big "if" has been replaced by the big "when" in the protocols of numerous medical centers in the United States.

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Still, as could easily have been predicted, far too many physicians have been little impressed or influenced by this giant step of surgical advancement. One of the important purposes of this paper is to reduce some of the unnecessary fears associated with the undertaking of this work, while arguing that open-heart surgery is entirely within the realm of a great many small city and community hospitals. It will be repeatedly pointed out that the possession of certain unpurchasable and intangible qualities will better determine its achievement than the physical plant and imposing props so often used as excuses for performance in some communities.

Availability of Case Material

The availability of patients will be determined by two factors: (1) the local incidence of recognized operable heart disease and (2) the cooperative efforts of regional colleagues in referring cases.

Incidence of Operable Heart Disease.—A completely acceptable estimate of the incidence of congenital heart disease in the general population is not yet available.[1] Most reports seem to be much too low. In view of the uncertainty of diagnosis and the widespread unfamiliarity with anomalous heart conditions, this is not surprising. Incidence reports from large series of births, postmortem examinations, and routine hospital admissions vary greatly (from 0.5 per 1,000 to 1.25 per 100). Figures based on routine examination of school children are also fallacious, since the highest incidence of death from congenital heart disease in any given year occurs during the first year of life.

Congenital and acquired heart disease occur with about equal frequency in the pediatric age group.[2] British authors report an over-all incidence of congenital defects of the heart of about 3 per 1,000 births and 1 per 1,000 at 10 years of age. Richards and associates,[3] reporting on 60,000 babies in New York City, place the figure at about 0.83%, including stillbirths. Lillehei and co-workers [4] state that about 50,000 infants born in the United States each year possess some form of anomalous heart. Considering present world-wide birth rates, this means that 2,000 infants with congenital heart disease are born every 24 hours.

Even more significant than mere figures is the fact that most of these infants possess correctable defects when techniques of open-heart surgery can be applied. Lillehei and co-workers [4] emphasize the all-important fact that, actually, less children are being given correction in a year, with present facilities, than are born eligible for operation within a given day. Though the figures are much less accurate than those for congenital lesions, a conservative estimate places at least 25,000 persons eligible annually in the United States for operation for acquired cardiac diseases.[4] This is all the more reason to reemphasize the need, the country over, for less complacency and apathy and more purposeful activity.

Keith and associates [5] report that congenital heart disease is the most common form of heart disease in infancy and childhood, rheumatic heart disease running second. Even a most superficial glance at any group of figures indicates the potential in terms of availability of clinical material. Indeed, the majority of patients arriving at the large medical centers have been sent from communities with inadequate facilities, some of them great distances away.

No colossal amount of graduate training will be required of the man in practice to recognize and properly channel patients suitable for more refined examination and possible operation. In the words of Osler: "The environment of a large city is not essential to the growth of a good clinical physician. Even in small towns a man can, if he has it in him, become well versed in methods of work, and with the assistance of an occasional visit to some medical centre he can become an expert diagnostician and reach a position of dignity and worth in the community in which he lives." [6] To know just what should be done is the first step; then to do it or get it done comprises the total philosophy of practical life. Convincing the practitioner, internist, and pediatrician in the community that local diagnostic and surgical facilities might be as good as those of the large city medical center is no painless and artless feat. We often speak of the need for laboratory space and materials, of aid and grants from this and that agency, but we so seldom openly speak of our most urgent needs: a genuine interest on the part of others within the medical precinct, unsolicited encouragement and reencouragement in the face of success and failure, purposeful and constructive discussion, and the offer of assistance and patient, understanding silence. The routine referral of available clinical material is a measure of final success; referrals during the trying days, when everything seems more potential than actual, are a measure of the faith and good will that make success inevitable. A man, or a team, in an unsettled environment cannot compose a peak performance.

Assembling a Team

One of the obstacles to be hurdled early in the course is the misguided notion that only by the assemblage of a vast throng of superscientists can this project be accomplished. Those who have not passed beyond proprietary literature and newspaper science are awed by the photographs depicting operating room scenes where, somewhere in the midst of the complex wilderness of gadgets and staff, is a patient undergoing open-heart surgery. The "pinball machine" effect would sometimes make a Rube Goldberg contrivance Arcadian by comparison. Nothing could be further from the truth.

To be sure, in some instances where a great deal of basic physiological data are to be obtained during the course of an operation, many recording and

measuring devices will have to be used. This, however, must be differentiated from the mere monitoring of a patient through the procedure when additional or superfluous data are not absolutely necessary. Simplicity should be the governing rule in any area where the prime interest revolves around the performance of an operation per se rather than the gathering of coincidental scientific data. Every individual, each control, every recorder, and all connections and lines are potential sources of hazard to the patient. No effort should be allotted to unnecessary gadgets or experimentation. The prime interest of the team at the community hospital is the operative intervention on an anomalous heart with the swiftest and safest route between the diagnosis and the accomplished operation. Fundamentally, a team need consist of two or three surgeons, one scrub nurse and her personal assistant or circulating nurse, one monitoring cardiologist, one pump "engineer" and his assistant, a laboratory technologist, and the anesthetist and his assistant. Each member of the team must be thoroughly indoctrinated in his role by repeated performance in the experimental laboratory long before the final move into the operating room. Disciplinary repetition in the laboratory has made each individual procedure as perfect and mechanical as that of eating a meal.

No matter how "simple" such devices as mechanical hearts may become, or how readily patients and colleagues accept the new technology, it is a foregoing truth that many hours will have to be spent by the surgical team subjecting themselves to the nurturing experiences gained only through repeated experiments in the laboratory.[7] "There is no more potent antidote to the corroding influence of mammon than the presence in a community of a body of men devoted to science, living for investigation and caring nothing for the lust of the eyes and the pride of life."[8] Of such material must a team ideally be constituted.

As part of the team it may well be necessary to include persons who are otherwise employed as engineers, physicists, steamfitters, and even veterinarians—anyone who can and will contribute a needed talent to the fulfillment of the project. A community is composed of a heterogeneous group of people of varying backgrounds and training. Much valuable aid can come from those who are so often willing to contribute to any purposeful effort. Indeed, this is a distinguishing feature of the community hospital setup. Repeated and motivated experiment, attention to minute details, the capacity for work before 9 a. m. and after 4:30 p. m. and Saturdays and Sundays as well, capacity for continued learning, the ability to keep from becoming too easily satisfied, the desire for progressive improvement, and many more intangibles, unpurchasable or obtainable by diplomas and degrees, are the necessary ingredients for a successful team. No amount of building space, grants-in-aid, or fancy and friable glassware will make it work.

Much debate goes on concerning the good and less desirable features of the various mechanisms available—bubblator versus diffusator, finger pump versus roller pump, heating versus cooling, or rubber versus plastic. Amid the confusing clamor there rises one unmistakable fact: some group, or groups, has made every kind of pump and oxygenator work within the justifiable region of safety. You cannot argue with success, and though one way may be somehow better than another there is the undisposable truth that the team is the most important single factor in success. Unsuccessful experiences will least and last of all condemn the human part of the mechanism.

Preliminary Experimental Experience

Mechanical heart-lung machines, though now flagrantly advertised in medical journals as seemingly "ready to use," cannot be bought and assembled like "do-it-yourself kits" and be made to work. Once assembled, the product becomes unlike any other on earth, appearance notwithstanding. No quantity of available funds can buy such a machine ready for use. There is much to be learned concerning its performance under every variable condition of temperature, flow-rate variation, and flow-volume conditions, the amount of oxygen required under any condition of flow, the adaptability to varying patient size, and a multitude of other inconstant details of performance.

The answers to the many basic factors to be learned are not all found in articles or in the results of any other man, machine, or group. There is no effortless or painless way of working out the obstacles and wrinkles; there is no pleasant and palatable way for arriving at even the simplest of principles that need to be understood. Work is the magic word; it is the open sesame to achievement. Without work, without the willingness to repeat experiment after experiment until there remain no unanswered questions regarding safety within reason, a man has no right to transport his equipment from the experimental laboratory to the operating room.

This does not mean that an impressive number of experimental successes need be on hand for reporting, though some seem to relate success to large sums of figures. We know of one group who operated on 140 dogs before a survival was achieved and of another who became repeatedly successful after the fifth animal experiment. There is no doubt in our minds that one group paid more attention to details than the other. No one doing experimental work in the community hospital, where animals, money, time, and effort may exist at a greater premium, can afford unnecessary waste in any direction. The prime motives should be not to design

some new freak, basically unlike anything else on earth, but to assemble an apparatus from units known to be useful and practicable and to get it to work so that the community can benefit positively from its presence. Alterations in design and expensive tool and die work should be left principally to the large centers where money, manpower, time, space, and available machine shops are accessories to routine performance.

To visit groups working elsewhere, to spend sufficient time with others who have pioneered and won success, will prove time-saving and effort-saving. It is also an inspiring experience to witness success. It is encouraging to watch another group successfully function together. It is a tonic beyond words to witness an aspiration of your own come true elsewhere—nothing else is more reassuring.

It is important to send all members of the team on such "tonic tours." Scrub nurses, private duty nurses, laboratory technicians—all have much to learn, and there is no learning that equals learning at first hand, which will prove an investment beyond decimal points and dollar signs. The day probably will never come when the perfect, tailor-made machine, devoid of human error in its mechanism and running, will be available. Those who sit idly by, waiting for this era, always find reasons for justifying idleness and poor performance. Progress has been the accomplishment of those who were ever fearful that they could not do enough and not of those who were afraid they were doing too much or more than their share.

Preoperative Evaluation and Selection of Patients

Again, illustrations and reports of monitoring appliances and recording apparatuses serve to confuse uninitiated minds. There is no intention to degrade, decry, or criticize the larger institutions that are doing an important job of gathering physiological data about disease. But a distinction must be made for the man in daily practice between the study of patients for purposes of attaining myriads of different academic data and the study of patients merely for making a working diagnosis. One actually needs to invest in only a few relatively simple pieces of apparatus to carry out the everyday needs for diagnosis and evaluation of patients for cardiac surgery. Aside from the routine studies (electrocardiograms, x-rays, and the usual laboratory tests), cardiac catheterization and, occasionally, angiocardiography are indispensable to the evaluation of the patient with congenital heart disease; such studies give sufficient data for a working diagnosis on which one can determine the need for surgery. Indicator dye dilution curves, phonocardiographic recordings, and electrokymography yield some additional data but may unnecessarily overburden the minds, pocketbooks, and available time of the part-time type of team which can be assembled in the community hospital.

After all, what precisely does the surgeon need to know other than a tenable diagnosis? Intracardiac and pulmonary vascular pressures and sometimes pulmonary arterial wedge pressure curves, pressure gradients across valve orifices, sites of shunts, and position of anomalous vessels are the basic preoperative requisites. With the dissemination of available, trained, thoracic surgeons, the stimulus is present for many small hospitals to incorporate these basic studies in their work-a-day protocol.

The most common error from the surgeon's point of view, associated with impatience to get started, is to select almost any kind of case for his initial efforts. Knowing that much is to be gained by a successful operation on a patient with an advanced cardiac problem, for whom there is no help from any other source, he is often willing to take the long chance—ignoring the fact that surgical failures have a more profound reverberation than medical failures. An early high mortality is much less tolerated at the community level, where criticism of new procedures is readily given. But the surgeon often finds himself in a whirlpool of confusion, being denied relatively "healthy" patients who can better tolerate the operative insult and being given the symptomatic cases which are the most impressive from the unreasonable clinician's viewpoint. A patient without symptoms is much more apt to be kept from the surgeon. In congenital heart disease it is much wiser to operate on existing pathology and not on the patient's symptoms.

Pulmonic stenosis (valvular and infundibular), interatrial septal defects, and pure interventricular septal defects without significant pulmonary hypertension constitute cases ideally suited for a beginning. Gradually, tetrology of Fallot, anomalous pulmonary venous drainage, acquired valvular heart disease, and others can be added as operative experience and acceptance are gained.

Some hospitals set up conferences comprised of members of the general staff to decide on the selection of cases. This is often fallacious from first thought, since such a group consists in the main of "voting members" who are ill-equipped, insufficiently interested, and unlearned in the field and who often gain very little from this real opportunity to learn. It is far better to set up a small group of genuinely interested men, internists, pediatricians, laboratory personnel, and the catheterization and surgical teams, to make these decisions. In this group there should be no room for the man who makes little or no earnest effort to acquaint himself with the fundamentals and who only visits the larger centers, availing himself of the voluminous written material and attending regional and national meetings. It has been stated that the clinical material can be found in the community, that the opportunity is always present, and that only work remains as a personal factor to be contended with.

Perplexities at the Beginning

Some intangible qualities of people have been stressed as the most important components of the various factors comprising the organization and functioning of a team. Lest one would be impressed wrongly that certain physical factors are of little consequence, a few words must be said concerning the importance of such tangibles as money and materials, space and time, and personal and personnel problems.

Most community hospital's and sources of funds for medical research are limited in comparison with the sizable grants and budgets of the larger centers. Being restricted, one cannot buy everything one would like to buy. This may not be such a handicap after all.

Much of our limited time and effort can be wasted on "gadgeteering." More than one great laboratory is arrayed with functionless expenditures, representing previous pursuits long since passed up for seemingly more worthwhile pursuits. The community hospital and the community can ill afford purposeless expense or the space to function as a museum.

One of the first principles, then, is to recognize the limitations of activities. A man who undertakes this project at the community level lives three distinct lives—one for the project, one for his practice, and one for his personal or family life. He becomes a part-time devotee to each. He is constantly faced with decisions as to which to devote himself to, since, when he decides on one, he automatically decides not to do another. His life becomes crowded with little or no time for refreshing unessentials; when lack of money or energy does not limit him lack of time does. He soon finds himself in the same dilemma as the youngster with a penny who wants one of each thing under the counter.

This is no doubt the most momentous task of all—to decide on the goal, strip it of unessentials, and then select the straightest and shortest route to its achievement, appearing unencumbered by a restricted budget, inadequate space, or disinterested and incredulous colleagues. The goal, of course, will be the creation of a relatively simple mechanism capable of maintaining extracorporeal circulation and oxygenation in the safest possible manner. There will be a limit to the sidetracking experiments and other pursuits which may only wind up with a self-satisfying bibliography.

Local and neighboring county and state divisions of the American Heart Association have proved most generous in granting financial aid to community hospitals undertaking such programs. Other organizations and clubs within the community are often likely sources of small annual donations, as well as hospital auxiliaries and interested individuals. The hospital and its administrators should consider the project an investment worthy of space and other resources. Indeed, without this interest there can be no beginning.

The difficulty is that the man or group needing the cash finds it an easy matter to think that others should be ready to part with it. It will take a lot of repeated efforts, speaking engagements, and other methods of public convincing that this, unlike other demands, is more than indiscriminating charity or giving. Every attempt must be made to make such drives for financial aid of an initiating and temporary nature, stressing the eventual creation of a self-sustaining and independent mechanism or one needing a minimal amount of aid for its sustenance. One of the best stimuli for convincing support is activity itself. A group already at work is more apt to receive help than one which spends time sharpening pencils, clearing desks, and waiting for an uninterrupted day, the mood, the money, or other desirables which seldom come without real effort.

Everything comes to him who hustles while he waits. Hours pass, days go by, and so do the years and even life itself finding men and institutions nursing intentions. One message, if nothing else, we wish to impart is this:

Given a trained surgeon and an interested and dedicated group of workers in a community hospital, there may be excuses but there are no real reasons why this newest surgical innovation cannot be added to the protocol. Postponement, the putting-off that usually waits for supposedly better times, circumstances, conditions, or machines, may cost the hospital an opportunity to take a giant scientific step forward. Patients, too, will be denied their rightful opportunity for this recent and effective treatment.

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SURGICAL INTERVENTION IN HEMOPHILIA

REVIEW OF THE LITERATURE AND REPORT OF TWO CASES

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Two surgical operations on patients with hemophilia are described. One was an appendectomy performed on a 26-year-old man with the laboratory findings and long history of hemorrhages characteristic of hemophilia. The other was a goniotomy in a 7-month-old boy with similar laboratory findings and a history of recent hemorrhages. In both patients the antihemophilic globulin (AHG) concentration was less than 1% on assay. Infusions of fresh plasma were given before operation in both cases, and in the second case assays for AHG showed that adequate levels could be achieved by such infusions provided the apparatus was siliconized, the plasma chilled, and the infusion given rapidly. In the older patient the postoperative course was marked by some bleeding, but both patients recovered.

Hemophilia is a disorder of blood coagulation resulting from deficient plasma levels of specific factors, the most common of which is antihemophilic globulin (AHG), followed in incidence by plasma thromboplastin component (PTC) and plasma thromboplastin antecedent (PTA). Characteristically, the clotting time in hemophiliacs is prolonged, with a normal bleeding time, prothrombin time, and platelet count; thromboplastin generation and prothrombin consumption are abnormal. Brinkhous [1] has classified hemophilia as (1) severe (classic) hemophilia, with essentially no AHG by assay; (2) intermediate hemophilia, about 5% AHG; (3) mild hemophilia, about 15% AHG; and (4) subhemophilia, about 35% AHG. The latter type usually gives a normal coagulation time.[2]

Morbidity and mortality in the hemophiliac undergoing surgery are high; even extraction of a tooth may lead to serious bleeding problems. Craddock and co-workers,[3] for example, reported three deaths in five hemophiliacs after major operations. This report is an analysis of the experiences of various authors relating to the problem of major surgery in the individual with hemophilia. To our knowledge there has been no survey of the literature on this problem since Craddock's in 1948. In addition, we are reporting two patients with severe hemophilia subjected to relatively serious surgical procedures.

Report of Cases

CASE 1.—A 26-year-old male student known to have classic hemophilia entered the University of California outpatient department in Los Angeles on July 15, 1958, complaining of recurrent dental abscesses. History included multiple recurrent hemarthroses and epistaxes beginning at age 8 months. Treatment had consisted largely of pressure to affected joints and immobilization. One blood transfusion when he was 2 years of age had caused a severe reaction and none had subsequently been attempted. Family history revealed no "bleeders" in five generations on the maternal side. However, clotting studies had not been performed.

Physical examination revealed an abscess of the lower right first molar tooth, with many other decayed teeth. There was little limitation of motion except in extension of the left knee. Pertinent laboratory findings were as follows: platelet count 117,000 per cubic millimeter (normal 200,000-350,000); coagulation time greater than 36 minutes; prothrombin time [4] was 10.5 seconds (100%); prothrombin consumption (Owren,[5] modified [6]) was zero; and thromboplastin generation (Miale and Wilson [7]) revealed deficiency of a plasma coagulation factor which corrected on substitution of normal $BaSO_4$-treated plasma. AHG concentration was less than 1% on assay.[8] X-rays revealed old arthropathy of both knees consistent with hemophilia.

The patient was scheduled for admission to the University of California Hospital, Los Angeles, for preparation for dental surgery. However, on the evening of Aug. 13, 1958, the patient entered the University of California Hospital emergency room complaining of anorexia, nausea, vomiting, and periumbilical pain of 30 hours' duration. Examination at this time revealed abdominal tenderness which gradually localized in the right lower quadrant, without guarding or rebound. The temperature was 39 C (102.2 F); rectal examination was unrevealing. The physical examination was otherwise as previously described. Urinary sediment contained 8-10 red blood cells per high-power field and 1-4 white blood cells per high-power field. The blood leukocyte count was 14,250 per cubic millimeter. Abdominal x-ray revealed a possible fecolith in the proximal appendix. A diagnosis of acute appendicitis with possible impending perforation was made, and, after considerable deliberation, operative intervention was elected. One unit (250 ml.) of fresh plasma was given intravenously over a period of 30 minutes, followed by a second unit which was allowed to drip during the operation. The clotting time was normal just prior to the operation, but, owing to lack of laboratory facilities at the late hour, AHG levels could not be obtained.

During surgery, which was performed by one of us (J. B.), all unnecessary trauma was avoided. The patient was given a general anesthetic without intubation. A right paramedian incision was made in the lower quadrant and bleeders tied with 0000 silk, with electrocoagulation of

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multiple small bleeding points. Serous fluid was encountered on entering the peritoneum. Immediately beneath the incision was a periappendiceal abscess enclosed in omentum, which was entered and suctioned. The omentum was dissected free proximal to the appendix with cautious clamping and ligation of the omental stump with 000 silk. The omentum was thus freed from the appendix and removed. The appendix was

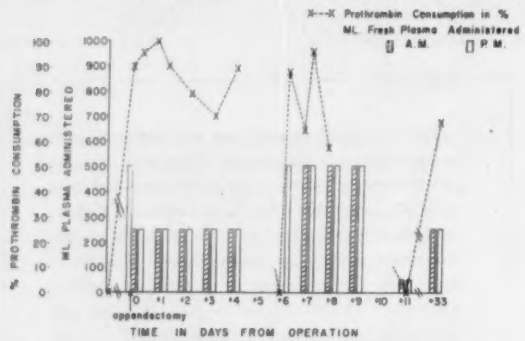

Fig. 1 (case 1).—Prothrombin consumption and plasma therapy in hemophiliac on whom appendectomy was performed.

then carefully dissected free from surrounding tissues and removed in the usual manner. Three minutes' observation revealed no bleeding. The rectus sheath was closed around a 0.25 in. Penrose drain. Subcutaneous tissue was closed with interrupted 0000 silk around a drain, a light gauze dressing applied, and the patient returned to the ward in good condition. Blood loss was estimated at 50 ml. Pathological examination of the specimen confirmed the diagnosis of acute suppurative appendicitis with focal acute peritonitis.

Infusions of plasma were continued postoperatively. Treatment and results of prothrombin consumption tests are summarized in figure 1. On the ninth postoperative day the patient complained of dyspnea. Venous distention, pulmonary rales, and hepatomegaly were noted. A chest x-ray revealed multiple patches of density in both lung fields. These findings were attributed to hypervolemia secondary to plasma administration. The patient improved rapidly with sodium restriction and interruption in plasma therapy for two days. On the 21st postoperative day slow oozing from the wound site was noted and a subcutaneous hematoma appeared. Several small bleeding points in the drain site were cauterized with silver nitrate and the hematoma was allowed to absorb. Hematocrit levels remained constant throughout. On the 31st postoperative day a draining peridontal abscess in the right mandible appeared and responded promptly to antibiotics. The patient was discharged in good condition on the 39th postoperative day. Dental extractions were postponed at the patient's request.

Case 2.—A 7-month-old male was admitted to the University of California Medical Center, Los Angeles, pediatrics department, for goniotomy procedure on Sept. 28, 1958. Previous admissions had revealed multiple anomalies, including congenital adrenal aplasia, glaucoma, and hemophilia. Hydrocephalus was also suspected.

The infant had had a hemorrhage from a femoral venipuncture site previously, and hematochezia had been noted. The family history revealed no other "bleeders." It was not feasible to do clotting studies on other members of the family. Positive findings included a head circumference of 44.5 cm.; ocular tension, with the patient under anesthesia, was 40.6 by Schiøtz's tonometer (normal—less than 25).

Blood studies revealed a plasma factor deficiency in the thromboplastin generation test corrected by $BaSO_4$-treated plasma, and AHG of less than 1% on assay. Serum electrolytes, initially markedly abnormal, were corrected when treatment for the endocrinopathy was instituted. AHG levels are summarized in figure 2.

After preoperative preparation with fresh plasma infusions, the child was intubated and general anesthesia used. Surgery was performed by Dr. Stephen Seiff. Examination showed the corneal diameters to be 13 mm. on each eye, with tension of 5 with a 10 weight bilateral (equal to 40.6 Schiøtz). There were no gross breaks in Descemet's membrane. Bridle sutures were then passed beneath the inferior, superior, and medial rectus with scant bleeding. Goniotomy was attempted in the right eye but the anterior chamber collapsed and the procedure had to be terminated. However, goniotomy was successful in the left eye. Oozing was minimal.

The infant made an uneventful recovery from the goniotomy with relief of increased intraocular pressure. Fresh plasma infusions were continued postoperatively. Management of the hemophilia is summarized in figure 2. Surprisingly low levels of AHG in the infant's blood even after infusions of plasma led to the discovery of unfortunate errors in preparation of the plasma, as will be discussed later. Adequate levels were achieved, however, in both the plasma for infusion and the patient's blood, when siliconized apparatus was used for collection, when the plasma was constantly chilled, and when administration was rapid.

Comment

Surgery in the hemophiliac has always carried with it a prognosis so serious that surgeons have avoided any operative procedures if possible. The table summarizes all case reports in the available literature of major surgery in hemophiliacs. Cases were included when they met the criteria outlined by Craddock,[3] namely, (1) laboratory findings of prolonged clotting time without abnormalities in other tests of the hemostatic mechanism, (2) positive family history, (3) history typical of hemophilia, and (4) occurrence in a male. In addition, most recent reports include assays for specific defects. It should be noted that all of the criteria do

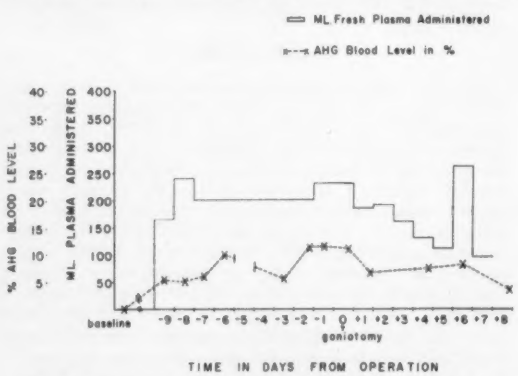

Fig. 2 (case 2).—AHG blood level and plasma therapy in hemophiliac on whom goniotomy was performed.

not apply to every case. In both of our cases, for example, family history was negative. Absence of a history of bleeding likewise does not preclude the diagnosis of hemophilia. However, previous episodes of hemarthrosis, bruising, hematuria, and

continued oozing from minor lacerations are found in most severe hemophiliacs and lend support to the diagnosis. Occurrence in the female is extremely rare.[9]

Of the 50 cases listed in the table, mortality from major surgery was 20%; the same mortality applies when only the 24 cases with laboratory-proved coagulation defects are selected. Intra-abdominal operations in 22 proved hemophiliacs of all types resulted in 3 deaths, a mortality of 13.7%. Among 12 hemophiliacs, appendectomy led to three deaths; 2 proved hemophiliacs of 7 undergoing surgery died, a mortality of 28.6%.

These mortality figures for hemophiliacs undergoing major surgery are approximately half those reported by Craddock,[3] and are also considerably lower than those of Friedrich in 1935.[10]

For appendectomy, the mortality figures are also approximately one-half of Craddock's figure of 66.6%.[3] The incidence of death in normal persons after appendicitis with rupture and peritonitis, who are treated conservatively and without operation, is 10 to 15%.[11] While hemophiliacs are known to suffer serious complications during conservative management, especially with infections,[12] nevertheless it appears that appendectomy in the hemophil-

*Major Surgery in Hemophilia—Reported Cases**

Authors	Date	Operation	AHG Deficiency Proved	Outcome	Remarks
This report	1958	Goniotomy	Yes	Recovery	
This report	1958	Appendectomy	Yes	Recovery	
Lisker et al.	1957	Appendectomy	No	Recovery	PTA deficiency
Gross et al.	1957	Splenectomy	Yes	Death	
Gross et al.	1957	Splenectomy	Yes	Recovery	
Gross et al.	1957	Splenectomy	Yes	Recovery	
Gross et al.	1957	Splenectomy	Yes	Recovery	
Kekwick and Wolf	1957	Radical abscess drainage	Yes	Recovery	
MacFarlane et al. [12]	1957	Laminectomy	Yes	Recovery	
MacFarlane et al. [12]	1957	Excision, hematoma	Yes	Death	Became anuric
MacFarlane et al. [12]	1957	Leg amputation	Yes	Death	Infection
MacFarlane et al. [12]	1957	Evacuation of clot	Yes	Recovery	
MacFarlane et al. [12]	1957	Mastoidectomy	Yes	Recovery	
Parks and Wass	1956	Resection of ileum	Yes	Recovery	
Jones and Knighton	1956	Laminectomy	Prob	Survived	Lab data not provided
Jones and Knighton	1956	Trephine, aspiration	Prob	Death	Lab data not provided
Jones and Knighton	1956	Packing, subdural space	Prob	Death	Lab data not provided
Remigy et al.	1956	Appendectomy	Yes	Recovery	
Meynell and Tudor	1956	Resection of ileum	Yes	Recovery	
Crevald	1956	Gastric resection	Yes	Recovery	
Crevald	1956	Trephine, evacuation	No	Recovery	PTC deficiency
Desmond	1955	Gastric resection	Yes	Recovery	
Eldin	1955	Gastric resection	Yes	Recovery	
Walker	1955	Partial gastrectomy	Yes	Recovery	
Lund	1950	Splenectomy	Prob†	Recovery	
Landry and Shoukimas [13]	1950	Appendectomy	Prob†	Recovery	
Craddock et al. [3]	1948	Appendectomy	Prob†	Death	
Vermooten	1948	Prostatectomy	Prob†	Recovery	Transurethral route
Vermooten	1948	Nephrectomy	Prob†	Recovery	
Wright	1948	Splenectomy	Prob†	Recovery	
Wright	1948	Resection, mandible	Prob†	Recovery	
Greene and Heck	1947	Prostatectomy	Prob†	Recovery	Transurethral route
Karitzky	1943	Débridement	Prob†	Recovery	
Vance	1939	Appendectomy	Prob†	Death	
Mertz and Meiks	1938	Nephrectomy	Prob†	Death	
Birch [14]	1937	Appendectomy	Prob†	Death	Pneumonia
Friedrich	1935	Splenectomy	Prob†	Recovery	
Friedrich	1935	Gastric resection	Prob†	Recovery	
Cloran	1935	Appendectomy	Prob†	Recovery	
Hays	1934	Tonsillectomy	Prob†	Recovery	
Henman	1933	Prostatectomy	Prob†	Recovery	
Blalock	1932	Amputation	Prob†	Recovery	Local hemostasis possible
Prima	1931	Appendectomy	No	Recovery	
Emile-Weil	1931	Appendectomy	Prob†	Recovery	Sex not reported
Emile-Weil	1931	Incision, Drainage	Prob†	Recovery	Local hemostasis possible
Emile-Weil	1931	Gastroenterostomy	Prob†	Recovery	
Wasnessensky	1930	Gastric resection	Prob†	Death	
Mathe and Mitchell	1929	Polypectomy, fulguration	Prob†	Recovery	
Hipsley	1923	Appendectomy	No	Recovery	
Pag	1913	Appendectomy	No	Recovery	

* Additional references to reports cited will be furnished by the authors on request.

† These cases in 1950 and earlier fulfill criteria outlined in text. However, since the thromboplastin generation test and AHG assay were not being done at the time, they can be listed only as "probables."

iac is attended by twice the mortality of conservative treatment. Morbidity is also higher in the hemophiliac in whom operation was done. In terms of length of hospitalization, hemophiliacs remain in the hospital an average of 34 days after appendectomy.[10] Normal persons with appendicitis but without rupture have a six-day hospitalization after appendectomy.[11a] Conservatively managed normal persons with appendicitis and abscess formation stay in the hospital only 20.6 days.[11a] Data on the conservative management of appendicitis in hemophiliacs are inadequate. In addition, many of the hemophiliacs studied had life-endangering hemorrhages during the prolonged postoperative course.

Management of hemophiliacs in recent years appears to be improving, an impression substantiated by the report of only 1 death in 17 recent intra-abdominal operations. There appears to be an increasing willingness to perform operations on hemophiliacs. Thus, of 45 cases in the literature, half were reported in the last decade.

Major surgical procedures in sites where local hemostatic measures are applicable present much less of a problem than internal operations.[14] For this reason, surgery involving extremities will not be discussed here. The use of local cooling measures to enhance vasoconstriction, and hemostatic substances such as fibrin foam placed into the wound, all help to induce coagulation. However, with bleeding into hollow viscera or into cavities, these measures are not applicable and the possibility of exsanguination is increased.

In case 1 several favorable factors applied: the patient's coagulation defect was known, permitting swift correction; fresh plasma was immediately available; and the appendix was easily mobilized through a bloodless incision. In spite of this good fortune, the patient developed a large hematoma at the operative site.

Both cases 1 and 2, particularly the latter, emphasize the importance of careful collection and rapid administration of blood or plasma. The blood must be collected rapidly in siliconized bottles or plastic bags, without foaming and with constant agitation so as to insure continuous mixing of anticoagulant and blood. Blood or plasma must be administered rapidly. Blood or plasma normally will vary greatly in its AHG content (50-150%), and on exposure at room temperature will lose AHG activity rapidly.[15]

Severe bleeding occurring in a hemophiliac treated carefully to attain a satisfactory laboratory AHG level is unfortunately a common problem. The prothrombin consumption test may also be misleading.[16] No satisfactory explanation can be offered for this lack of correlation until more detailed understanding of the interaction of the various components in forming thromboplastin is achieved. It must be remembered that time alone will determine the prognosis in the hemophiliac undergoing surgery and not necessarily the results of clotting studies. Hypervolemia from plasma administration is a complication occasionally encountered in hemophiliacs. This problem may be managed with exchange transfusions of fresh whole blood or plasma, or concentrates of human or bovine AHG may be used.[17] Unfortunately, bovine AHG preparations are not readily available in the United States, and pooled plasma concentrates carry the risk of infectious hepatitis. Fraction 1 of Cohn, containing a high concentration of AHG, may be of help but varies considerably in potency and may also transmit viral hepatitis. Much work is needed to provide better replacement therapy.

Another complication is the development of a circulating anticoagulant as described by Lawrence and Johnson. This is a grave development and is extremely difficult to handle.

Summary

Two known hemophiliac patients survived operative procedures, one for appendectomy and one for goniotomy. These cases emphasize the importance of careful collection and rapid administration of blood or plasma. Although laboratory methods for the assessment of hemophilia are still inaccurate, management of hemophiliacs in recent years appears to be improving. Of 50 cases in the available literature of persons suspected of having hemophilia and in whom major surgical procedures were performed, mortality was 20%. In 24 such cases with proved hemophilia there was a similar mortality. A mortality of 28.6% was found for appendectomy in proved hemophiliacs. In spite of the better preparation and treatment of the hemophilic surgical patient in recent years, any operative procedure in a hemophiliac remains a grave undertaking.

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Dr. Jeanette Schulz granted permission to report case 2.

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TREATMENT OF PARALYSIS AGITANS WITH CHLORPHENOXAMINE HYDROCHLORIDE

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Chlorphenoxamine was administered to 25 patients with paralysis agitans in a preliminary test to determine dosage and observe side-reactions. Thereafter it was administered to 136 patients who had been treated unsuccessfully with other drugs. It allayed tremor only in the occasional patient, and in some the tremor was accentuated. Its most consistent effect was on akinetic, tired, weak patients, who were enabled to move with greater celerity, strength, and endurance. It stimulated without inducing excitement and relaxed without causing flaccidity or enfeeblement. Three case histories illustrate its effects on the disabling symptoms of the patient. The side-effects observed were neither frequent nor serious. Tolerance did not seem to increase with lapse of time, and the favorable effects continued only as long as the drug was administered.

Argument is often heard that we have more than enough compounds for the treatment of paralysis agitans (Parkinson's disease), and some even claim that hyoscine hydrobromide alone can suffice for the care of all the symptoms of this disease. The fact remains that, despite the addition during the past decade of a half dozen new synthetics—trihexyphenidyl (Artane) hydrochloride,[1] cycrimine (Pagitane) hydrochloride,[2] procyclidine hydrochloride (Kemadrin),[3] benztropine (Cogentin) methanesulfonate,[4] ethopropazine (Parsidol) hydrochloride,[5] and orphenadrine (Disipal) hydrochloride[6]—to the older belladonna preparations, those who treat large numbers of patients who suffer from paralysis agitans feel a dire need for more and better compounds, for various reasons: 1. Many patients, especially those suffering from tremor and akinesia, are not helped sufficiently by current drugs. 2. People live longer; hence we see increasing numbers of older patients, many of whom cannot tolerate the available remedies. 3. Drugs tend to lose their beneficial effects with the passing of time, so we must have a large assortment of good compounds for replacement. 4. Some patients tire of any remedy during the long siege of the illness and are forever in search of something new. 5. There are increasing indications that neurosurgery is likely to fail in its anticipated promise of relief, so patients in the foreseeable future will of necessity have to rely on medication for any benefits they are to derive from treatment.

This paper will introduce a new drug, chlorphenoxamine hydrochloride, that has proved beneficial to many of our patients whom standard

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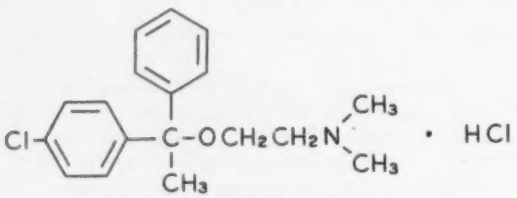
agents for paralysis agitans failed to help. It has been in use in Germany for several years after prior establishment of its therapeutic safety.[7]

Chlorphenoxamine is beta-dimethylaminoethyl (p-chlor-alpha-methyl-benzhydryl) ether hydrochloride. Chemically, it is a derivative of diphenhydramine (Benadryl) hydrochloride, with structure as shown in the figure.

The addition of a p-chlor atom or an alpha-methyl group to the beta-dimethylaminoethyl benzhydryl-ether molecule lessens the antihistaminic action of the compound and increases its anticholinergic action. The addition of both elements serves to accentuate this action. The oral LD_{50} dose in mice is 410 mg. per kilogram, which indicates a high index of safety. Pathological studies of animals that had been fed chlorphenoxamine for long periods failed to reveal any abnormalities in the organs or blood constituents. Hemogram studies in 20% of our patients and cephalin flocculation, thymol turbidity, and urinalysis studies in eight of these patients were all reported normal.

Clinical Material and Procedure

Chlorphenoxamine was supplied to us to determine its possible usefulness in the treatment of this disease. It was provided in the form of



Chlorphenoxamine hydrochloride.

100-mg. capsules and 50-mg. coated tablets. The tablet was found to be more practical and better tolerated and is the form we have continued to use.

The study began with a group of 25 specially selected patients, with the aim of establishing the effects, side-reactions, and range of therapeutic dosage. Some patients, known to possess a high tolerance for drugs, used as much as 600 mg. per day without evidence of side-reactions. Others reported satisfactory results from only 25 mg. of chlorphenoxamine, three times daily, achieved by cutting the tablet in half. However, it became evident early in the study that the optimum dosage for most patients was about 50 mg., three times daily. Some fared better on 100 mg., three times daily, especially the younger postencephalitic patients. It was found better tolerated after meals, with milk, because a few patients complained of indigestion when it was taken with water. There was little occasion for increasing the dosage, as patients tended to remain on therapy with the same amount of drug month after month, indicating that there is little increase in tolerance. In cases where such increase did occur, it was usually after three to six months of use, and the addition of one or two tablets per day served to restore the initial benefits.

The preliminary group of 25 patients was steadily expanded to include 161 patients with paralysis agitans, who were selected only to the extent that they had failed to derive sufficient benefits from other drugs. Among those were 96 males (60%) and 65 females (40%). The youngest was 38 years of age and the oldest 76. In addition to the patients with paralysis agitans, six with senile tremor, three with hereditary chronic progressive chorea with mental deterioration (Huntington's chorea), three with familial hereditary tremor, one with dystonia musculorum deformans, one with hemiballismus, and one with torticollis spasm were likewise studied for the effects of chlorphenoxamine.

The new compound was used alone in 67 patients and was combined with other drugs in 94. Comparisons were made of its action with those of well-known drugs and with placebos. Objective studies were conducted with 12 patients in the laboratory by means of electronic instruments specifically designed for measuring changes in rigidity and tremor.[8]

On the basis of the above studies, clinical observations, and reports from the patient and family, the results of treatment with chlorphenoxamine were classified as failures if no benefits accrued to the patient, if the therapy was discontinued because of side-reactions, or if the patient had not been heard from for more than two months, which meant the allotment of medicament had been exhausted and the patient was dissatisfied. Patients were regarded as "failures" even if they had been on the drug therapy but one day. Since no patient was actually made "worse" by the medicament, no such classification was deemed necessary. The successful results were grouped under the one heading of "improved," because experience has shown that in paralysis agitans it is not desirable to delineate fine shades of change, since the symptoms and behavior of the patient are often influenced by emotional and situational factors and they can vary from day to day.[9] Doubtful and borderline changes were not counted among the successful results. Moreover, no patient was classified as "improved" unless chlorphenoxamine had been used with favorable effects for at least two months.

Results

On the basis of the stated criteria, the results of treatment with chlorphenoxamine are recorded in table 1. It is noted that 53% of the patients were improved. Among those were many who were

remarkably benefited by the new compound. The low incidence of disturbing side-reactions made it even more acceptable to the patients. The favorable results were about equally distributed among the older and younger patients (table 2). Thus, 28 (49%) of 58 patients in the 61-70 age range were improved as compared to 15 (55%) of 27 patients in the 41-50 age range. This finding bears special significance, considering that the group of patients with paralysis agitans is becoming increasingly older [10] and that such patients are usually hypersensitive to drugs; hence they respond less favorably than younger patients.

TABLE 1.—*Results of Treatment with Chlorphenoxamine Hydrochloride in 161 Patients with Paralysis Agitans**

Disease Type	Unimproved	Improved	Total
Postencephalitic	14	15	29
Arteriosclerotic	33†	27	60
Idiopathic	29‡	43	72
Total, No.	76	85	161
Total, %	47	53	100

* Fifteen additional patients (6 with senile tremor, 3 with familial hereditary tremor, 3 with hereditary chronic progressive chorea with mental deterioration, 1 with dystonia musculorum deformans, 1 with torticollis spasm, and 1 hemiballismus) were treated with chlorphenoxamine. Only those with hereditary chronic progressive chorea and hemiballismus responded favorably.
† One patient died from a gallbladder operation. Another underwent ultrasonic surgery, so that chlorphenoxamine therapy had to be discontinued.
‡ One patient died from severe burns.

The 47% failures were in large measure accounted for by patients who had tremor as the predominant symptom or those in whom a minimal tremor became accentuated by the drug. Some failures were accounted for by patients who had failed on therapy with all other compounds because of neurotic or unstable components of personality. Still other failures occurred among patients who, through long usage, had become dependent on trihexyphenidyl, cycrimine, or procyclidine hydrochloride and were generally distrustful of a new compound. A few discontinued use of chlorphenoxamine because of genuine concern about side-reactions, such as indigestion, especially where there had been a history of gastric ulcer. Some have not been heard from, and the reason for their dissatisfaction remains unknown.

Aside from numerical findings, the day-to-day experience with the patients served to confirm the outstanding quality of the new product. Not only were the reports highly gratifying but there was a pronounced demand from the patients and family for the drug, to an extent where it was hardly possible to maintain a sufficient supply month after month. This was in sharp contrast to our experience with 10 other new compounds which were being tested at the same time as the chlorphenoxamine. There was no comparable interest in any of the other drugs. Thus, apart from all other considerations, the consistently great demand for chlorphenoxamine was conclusive proof that it was helping the patients more than the other experimental drugs and more than some of the standard agents which they had formerly used.

Chlorphenoxamine exerts a gentle yet potent action, entirely different from that of the parent compound, diphenhydramine. It has a muscle relaxant action far above that of diphenhydramine and also an energizing and stimulating action, without induction of excitement or agitation. Patients are able to move faster and more freely and with greater strength and longer endurance. It helps to loosen rigid muscles, and it successfully counteracts akinesia, tiredness, and weakness. While in an occasional patient it served to allay tremor and excitement, it had the least satisfactory action against tremor, which in fact it tended to accentuate in 16 patients when used alone. However, with addition of ethopropazine or diphenhydramine it was found possible to keep tremor under satisfactory control, sometimes even with the addition of small doses of trihexyphenidyl.

Chlorphenoxamine helped to relax spasm and cramps of somatic origin and was especially beneficial to those who suffered from visceral spasms, or so-called inner tension and tremor. Some patients with frequency and urgency of urination obtained striking relief from its use. The muscle relaxant action is seemingly of a gentle nature, since even in large doses there was no evidence of enfeeblement or flaccidity. The usual duration of action was four to six hours and the onset of action about 30 minutes. However, a few patients were maintained comfortably on one tablet a day.

A number of patients (67) found it possible to discontinue use of all former remedies and to function successfully in their occupations and everyday activities with use of chlorphenoxamine alone. Others found it more advantageous to combine it with trihexyphenidyl (30 patients), benztropine methanesulfonate (25), procyclidine (12), cycrimine (10), ethopropazine (10), and diphenhydramine (5). It combines readily with all agents used for paralysis agitans. Of the 15 patients with extrapyramidal syndromes not associated with paralysis agitans, only the patient with hemiballismus and the two with hereditary chronic progressive chorea with mental deterioration responded favorably.

TABLE 2.—*Age of Patients in Relation to Results of Chlorphenoxamine Treatment*

	Age, Yr.					Total	
Type of Results	31-40	41-50	51-60	61-70	71-80	No.	%
Unimproved	2	12*	23†	30‡	9	76	47
Improved	2	15	34	28	6	85	53
Total	4	27	57	58	15	161	100

* One patient died from severe burns.
† One patient underwent ultrasonic surgery and chlorphenoxamine had to be discontinued.
‡ One patient died from a gallbladder operation.

Report of Cases

Chlorphenoxamine was so effective in most patients with paralysis agitans that it is considered desirable to submit several illustrative cases that, in addition, will provide details of the administration, dosage, and side-effects.

CASE 1.—A 57-year-old man had idiopathic paralysis agitans. In 1949 he began to experience some difficulty in writing. This was followed by tremor and rigidity of the right arm and leg, which rapidly spread to involve the trunk and left limbs. In addition there was marked akinesia; frozen facies; labored speech; and contractures in the spine, neck, and limbs. He could not dress or feed himself without assistance, and when he was placed on his feet, his gait was propulsive and he tended to fall. He became totally disabled for work in 1955. Therapy with a variety of drugs, including trihexyphenidyl, benztropine methanesulfonate, cycrimine, and orphenadrine, in turn, had been tried, but his tolerance was poor and he rejected all medicaments on complaint of dryness and mental fogginess. For the past three years he had relied almost entirely on physiotherapy for relief. In June, 1958, therapy was started with a 100-mg. capsule of chlorphenoxamine, three times daily, and when seen a month later he showed remarkable change. His mind was sharper, his movements freer, and his gait steadier, and he was able to smile and talk. There was a release of automatic movement so that he was able to get out of a chair with ease and spontaneity. He then began to take two 50-mg. tablets three times a day and has continued to the present in a more vigorous, active, and happier state than he has been in many years. There have been no side-reactions.

This man could not tolerate standard agents and yet found it possible to accept large doses of chlorphenoxamine with benefit and without a single complaint of side-reactions. A euphoric element appeared among the effects in this as in many other cases. It is difficult to be certain whether this is a direct action of the drug or whether it is secondary to the physical improvement. It would seem to be primary.

CASE 2.—A 55-year-old woman had suffered from postencephalitic paralysis agitans since 1925, when drowsiness and tremor of the right hand appeared. During succeeding years came rigidity of the trunk and right limbs, sialorrhea, drooling, and monotone speech. Vaccines were tried without avail and, later, massive doses of atropine and Bellabulgara. More recently, trihexyphenidyl was used, but by 1956 contractures appeared in the neck, spine, and legs, and the body became bent. Rigidity and akinesia progressed to a point where the patient was barely able to get out of a chair, and her gait became propulsive and stumbling. Other preparations were tried, among them benztropine methanesulfonate, cycrimine, and orphenadrine, with only temporary relief, and the patient returned to therapy with trihexyphenidyl. In April, 1958, 50 mg. of chlorphenoxamine, three times daily, was added to the 10 mg. of trihexyphenidyl, three times daily. The effect on tremor, rigidity, akinesia, and drowsiness was dramatic. Her mind sharpened, she moved with greater speed and freedom, and her speech became clearer. She was able to get in and out of bed; before she had been unable to do so. She felt stronger and happier. In August she ran out of her allotment of chlorphenoxamine and again became rigid, with her body bent, and in an effort to get out of bed she fell and injured her side and head. On continuing therapy with chlorphenoxamine, she regained the original improvement and has continued to do well.

The above case illustrates the manifold actions of the new compound, even against tremor. It especially points up the fact that when medication is discontinued, all benefits cease; hence the need for continuous medical supervision and treatment of patients with paralysis agitans.

CASE 3.—A 60-year-old man suffered from idiopathic paralysis agitans of eight years' duration. His chief problem was tremor of the left arm, with increasing rigidity in the left limbs. He was sensitive to all medicaments, and even small doses caused nausea and dryness and made him feel "dopey" and weak. In February, 1958, therapy with 50 mg. of chlorphenoxamine was tried with 1 mg. of benztropine methanesulfonate, twice daily. After a week he complained of indigestion and an upset stomach. The chlorphenoxamine therapy was discontinued. A month later it was tried without benztropine methanesulfonate and the effect was "marvelous." He became more relaxed and stronger, and his appetite improved. "If I could only stay this way for the rest of my life" was his comment. He has taken chlorphenoxamine, 50 mg. three times a day, for the past seven months and there have been no further complaints of indigestion.

The above case shows the lasting good effects of chlorphenoxamine and indicates that it can be used alone to better advantage in some sensitive patients than when combined with other compounds.

An instance of failure and a common problem are illustrated in case 4.

CASE 4.—A 63-year-old man had bursitis of the left shoulder three years ago; it improved with x-ray treatment. Shortly after came a general slowing down of the body and a shuffling, stumbling gait. His left arm, and later the right arm, became tightened and drawn upward across the abdomen. He was given a diagnosis of arteriosclerotic form of paralysis agitans. He was treated with 2 mg. of trihexyphenidyl, three times daily; he discontinued this therapy after a week because of dryness and mental confusion. Later therapy with a combination of 1.25 mg. cycrimine and 25 mg. of phenindamine (Thephorin), three times daily, was tried, which after a favorable interval had to be abandoned because of complaints of "dopiness," dryness, and blurring of vision. He returned to therapy with one tablet of trihexyphenidyl a day. By this time tremor appeared in his arms, and he was placed, in turn, on therapy with ethopropazine, diphenhydramine, and hyoscine, to all of which he was sensitive. In August, 1958, he experienced cramps in his legs. Benztropine therapy was tried and had to be discontinued because of mental confusion. He was thereupon given 50 mg. of chlorphenoxamine, three times daily, after meals. He reported that the first tablet made him very drowsy and that the second tablet put him to sleep "for two days" so that he could not work in his candy store. He returned to therapy with one tablet of trihexyphenidyl per day, which could not possibly combat his advanced symptoms.

Here we could see neurotic and hypersensitive components in the personality operating as severe obstacles to better therapy.

Side-Reactions

There was not a single instance of dangerous or toxic effects among the 161 patients with paralysis agitans under treatment with chlorphenoxamine. Such side-effects as occurred from its use were of minimal degree and of no greater frequency

than those encountered with standard agents. Ten patients complained of indigestion; eight, drowsiness; six, dryness of the mouth; four, nausea; four, dizziness; and two, anorexia. A total number of 28 patients (17%) offered a total of 34 complaints. Chief among the complaints were indigestion, drowsiness, and dryness of the mouth. The indigestion was largely corrected by having the patients take the medicament after meals and with milk instead of water.

It is of interest that no objective pupillary changes occurred, even among patients who were using as much as 600 mg. of chlorphenoxamine a day; nor was there a single complaint of blurring of vision. On this basis, chlorphenoxamine may be considered an ideal drug to use in patients with paralysis agitans who also suffer from glaucoma.

Comment

We stand in great need of drugs that will successfully counteract akinesia, adynamia, mental sluggishness, and lack of mobility in patients with paralysis agitans. In fact, some neurosurgeons have reached a decision not to operate in such situations, because even after reduction or elimination of rigidity and tremor the patients are almost as disabled as they were before the operation. While we possess several drugs that can combat these symptoms, it so happens that orphenadrine has a tendency to lose its good effects rather rapidly in some patients; dextro amphetamine (Dexedrine) sulfate often causes excitation and disturbing palpitations; methylphenidate (Ritalin) hydrochloride helps an occasional patient only when used in large doses of 20 or 40 mg.; and amphetamine (Benzedrine) sulfate causes cardiocirculatory reactions in the older patients.

In this setting, chlorphenoxamine has proved a valuable addition to current remedies because it exerts a gentle, stimulating action that continues month after month in a high percentage of patients in whom it proves effective. It is especially good to use in patients in whom the effects of orphenadrine have worn off. It affords energy, greater freedom of motion, more strength of body, and a general feeling of well-being that lasts throughout the day. True, it does not perform as would be desired in all cases, but then no drug has yet been discovered that is effective in 100% of patients with paralysis agitans. Experience has shown that if a new drug provides 30% of patients greater benefits than they were able to obtain from available compounds, it has clinical merit. Because chlorphenoxamine is a nontoxic compound and because it affords relief to 53% of patients who were insufficiently helped by current remedies, it is a worthy addition to the armamentarium of preparations for paralysis agitans.

Summary and Conclusions

A new drug, chlorphenoxamine, has been shown by studies abroad and in our own series of 161 patients with paralysis agitans to be free of toxic effects. It has positive value in the treatment of the disease. It is especially effective against rigidity, akinesia, fatigue, depression, and weakness, but less against tremor. It provides the patient with more energy and strength, greater freedom of motion, and longer duration of activity than most current remedies. Increased tolerance is comparatively rare and does not appear before three to six months of use. The method of administration and posology are presented and illustrated by case records. The side-reactions are minimal. It is of little benefit in non-Parkinsonian extrapyramidal diseases. The findings indicate that chlorphenoxamine is a valuable addition to the armamentarium of drugs for use in patients with paralysis agitans. It can be used alone or with other agents, such as trihexyphenidyl (Artane) hydrochloride, cycrimine (Pagitane) hydrochloride, procyclidine hydrochloride (Kemadrin), benztropine (Cogentin) methanesulfonate, or ethopropazine (Parsidol) hydrochloride.

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The chlorphenoxamine used in this study was supplied by the Pitman-Moore Company, Division of Allied Laboratories, Inc., Indianapolis. It will be marketed under the trade name of Phenoxene.

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CLINICAL NOTES

STATISTICAL METHOD FOR DETERMINATION OF OVULATION TIME IN WOMEN

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The data developed by Sevag and Colton for their paper "Simple Chemical Method for the Determination of Ovulation Time in Women," which appears in this issue of THE JOURNAL, page 13, offer the opportunity to test the possibility of applying a simple technique of linear correlation to estimate the day of ovulation. The data studied were limited to normal full-term pregnancies where conception was achieved by therapeutic donor insemination. In addition, all patients having menstrual cycles of less than 23 or more than 34 days were eliminated from consideration. Data beyond these limits appeared to be sufficiently unusual as to warrant their exclusion from a study that seeks to determine whether any typical relation exists between the length of the menstrual cycle and the day of ovulation.

Average Length of Menstrual Cycle and Day of Ovulation for Sixty-seven Women

	Average Length of Cycle in Days, No. of Women											
Day of Ovulation	23	24	25	26	27	28	29	30	31	32	33	34	Total
10			1	2									3
11			1	3	2	3		1					10
12	1		1	3	1	6	1	1		1			15
13					2	6	4	3		1	1	1	18
14						4	3	3	3	2		1	16
15									2			1	3
16							1				1		2
Total	1	0	3	8	5	19	9	8	5	4	2	3	67

Sixty-seven patients met the criteria concerning manner of conception and length of the menstrual cycle. These patients had a mean cycle length of 28.7 days and a mean day of conception of 12.8 days as compared with 29.0 days and 12.7 days, respectively, for all cases in which conception took place. The table presents the cases of these patients, classified on the basis of the average length of the menstrual cycle and the day on which conception occurred.

With the average length of the menstrual cycle as the independent variable the following measures are obtained: regression equation: $Y_c=2.2+0.37X$; standard error of estimate, 1.1; and coefficient of correlation, 0.63. In using this regression equation the average length of the menstrual cycle is substituted for X, and the Y_c value obtained indicates the likely day of ovulation. It may be expected that approximately two-thirds of the cases will lie within a range of $\pm$ 1 standard error of estimate. The coefficient of correlation, which in this case differs significantly from zero, is an indication of the relationship or association between the average length of the cycle and the day of ovulation.

To illustrate the use of these measures let it be assumed that a woman has an average menstrual cycle of 30 days. Substituting this for X in the equation gives day 13.3 for Y_c, i. e., ovulation is most likely to occur during the 13th day. The standard error of estimate indicates that in approximately two-thirds of the cases ovulation would occur for such a person not earlier than day 12.2 nor later than day 14.4.

From these statistical measures several observations can be made. First, the data tend to confirm the findings of Sevag and Colton that ovulation (as judged by successful inseminations) occurs between the 10th and 15th day for nearly all cases regardless of the length of the menstrual cycle. Using the extremes of length of the cycle for the 67 cases studied, 23 days and 34 days, the range of the day of ovulation runs from 10.7 to 14.8, i. e., essentially the same results as the Sevag-Colton paper indicate. Second, the amount of change in the day of ovulation for a one-day change in the average length of the menstrual cycle is slightly more than one-third of a day.

Meaning of Statistical Measures

The value of the regression equation that has been developed lies in the fact that it permits one to determine the probable date of ovulation when

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the chemical procedures described in the Sevag-Colton article are not available. Although in their article they indicate that ovulation seems most likely to occur between cycle days 10 and 15, the use of the equation permits a more critical determination that takes account of the length of the menstrual cycle, e. g., for a 24-day cycle ovulation can be expected on day 11.1, whereas for a 32-day cycle the day of ovulation might be expected to be 14. For the person interested in determining dates in the absence of the availability of chemical tests such variation could be of significance.

FEBRILE REACTION TO PROCAINAMIDE THERAPY

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Since procainamide (Pronestyl) was introduced in 1950, four instances of febrile reactions to this drug have been reported. Review of these and details of another well-documented case are presented in order to delineate the characteristics of the reaction and the type of investigation necessary to establish the diagnosis with a reasonable degree of accuracy.

In each of these cases, the appearance of the febrile reaction was rather prompt. It occurred within the first 24 hours after administration of the drug and it disappeared within 24 hours after the drug therapy was discontinued. The appearance of fever and general malaise in patients with recent myocardial infarctions in two of the cases reported led to investigation for cause of the fever other than the presence of a febrile reaction due to the drug. This is likely to be the course taken under circumstances that were present at that time, and, if it is not borne in mind that febrile reactions to procainamide can occur, such investigations may be extensive and futile. When discontinuation of the drug therapy is followed by clearing of the febrile reaction, one cannot assume that this is proof of a febrile allergic drug reaction. After the symptoms have been reproduced on administration of the drug and seen to disappear on discontinuation of administration for a total of three occasions, it is reasonable to conclude that one is dealing with an allergic febrile reaction. Myocardial infarction is a serious illness and complications deserve serious consideration. The clinical picture and investigation of such a reaction to procainamide therapy are illustrated in the following case report.

Report of a Case

A 61-year-old male was admitted to the hospital on Feb. 15, 1957, because of progressive dyspnea of about two months' duration. He had been hospitalized in January, 1952, with an acute myocardial infarction. During that hospitalization he had numerous premature ventricular contractions and was given procainamide, 500 mg. every four hours, or every six hours, for a period of four weeks. The drug therapy was discontinued after four weeks. He had been hospitalized later because of symptoms of angina pectoris and was found to have a low cardiac reserve.

On admission, physical examination revealed moist inspiratory basal rales, moderate cardiac enlargement, and a trace of ankle edema. He was observed to have frequent premature contractions, which on electrocardiographic study were demonstrated to be ventricular premature contractions. The signs and symptoms of congestive heart failure disappeared on bed rest, a low-sodium diet, and an occasional injection of meralluride (Mercuhydrin). On March 6, 1957, procainamide therapy, 250 mg. every six hours, was begun because of the premature ventricular contractions. On March 7, he had a chill and for the next 11 days felt poor generally. He complained of weakness, anorexia, general malaise, and febrile sensations, and he had run an elevation of temperature almost constantly. On March 18, the drug therapy was discontinued and within 24 hours the patient felt much better. His appetite improved, and he no longer complained of generalized aching and sensations of fever. His temperature became normal.

On three subsequent occasions the patient was given procainamide with definite febrile responses beginning about 12 hours after the first dose. The procainamide was given in doses of 250 mg. every four hours for a variable number of times. When he was given only 250 mg. for one dose, he did not have any reaction. If it were given for two doses, he would have a chill and fever. Dummy capsules of the same appearance but containing lactose did not give a similar reaction. To document the febrile

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reaction clearly, the patient's temperature was taken every four hours day and night. During this time it ranged between 96.2 and 98.0 F (35.7 and 36.7 C). No change in temperature or symptoms appeared on administration of the dummy capsules, but when he was given procainamide, 250 mg., at 8 a. m., and this was repeated at noon, a chill was experienced at about 9 p. m. His temperature was 101 F (38.3 C) at 12 midnight, 100 F (37.8 C) at 4 a. m., and normal at 8 a. m. and remained normal for the next two days.

The patient declared that the first sensation of the reaction was a tingling and generalized feeling of nervousness, followed by general malaise and nausea. At the same time he would develop a definite diuresis. When he was observed at these times he appeared to have peripheral vasoconstriction. His skin was pale and moist. Chill and fever then appeared. He had no diarrhea and no vomiting; his blood cell count did not change. Procainamide did not have any appreciable effect on the premature ventricular contractions. Results of a patch test were negative to procainamide. Further skin testing was not done, since it is well known that skin tests are not reliable in drug reactions of this type.

Comment

The first report of febrile reactions to procainamide was by Leibowitz[1] in 1951. He reported the case of a 48-year-old businessman with episodes of tachycardia not responding to quinidine. The patient was given 500 mg. of procainamide four times daily, and within a week he reported experiencing weakness and sweating during the day and shaking chills and fever in the evenings. He stopped taking the drug and suffered no further chills and fever until he was advised to reinstate the medication and within 24 hours experienced another shaking chill. Procainamide administration was discontinued and within 24 hours his temperature was normal. Attempts to induce him to take it again were unsuccessful.

In August, 1952, two cases of febrile reaction to procainamide given orally because of premature contractions were reported.[2] One of the patients had had a recent posterior myocardial infarction and was on anticoagulant and procainamide therapy.[2a] An unusually high temperature was noted for five days, and anticoagulant and procainamide therapy was discontinued with the result that within 24 hours the temperature was normal. Improvement in the patient was said to be immediate and dramatic. Aching and malaise, as well as nausea and apprehension, had been experienced, and these were no longer present within 24 hours after the drug therapy was interrupted. Two days later, the patient was given 250 mg. of procainamide at 10 a. m. and by 4 p. m. that afternoon was uncomfortable and irritable and had a temperature of 104 F (40 C). A total of five doses of 250 mg. of procainamide every four hours was given and then the therapy was discontinued. The next day the patient felt normal again and remained so for five days. The therapy was then resumed for the third time, and after the third dose she again developed fever with a maculopapular itching rash. After discontinuing administration of the drug, symptoms disappeared promptly.

The second patient[2b] was a 53-year-old male with hypertension of 20 years' duration who suddenly developed substernal pain and was found to have an acute anteroseptal infarction pattern on an electrocardiogram. He was immediately given a dose of 1.5 Gm. of procainamide orally because of premature contractions. This was followed by 250 mg. of the drug every four hours. After the third dose the patient developed a generalized maculopapular erythematous rash with severe itching, nasal congestion, slight generalized lymphadenopathy and a temperature of 102 F (38.89 C). Procainamide therapy was discontinued and diphenhydramine (Benadryl) given every four hours. His symptoms disappeared within 24 hours. The patient was receiving other medicines at the time of the reaction so he was given procainamide three months later. After the fourth dose of 250 mg. every four hours, the same reaction occurred, and the therapy was discontinued. Results of a patch test were negative.

In December, 1952, McGarry[3] reported the case of a 57-year-old man with an acute myocardial infarction who, after being placed on therapy with 500 mg. of procainamide every four hours from the 5th day after infarction until the 20th day, showed a temperature range between 101 and 103 F (38.33 and 39.44 C). After the procainamide therapy was discontinued there was prompt defervescence and striking subjective improvement. After the patient had been feeling well for 72 hours, a test dose of 500 mg. of procainamide, given orally, produced a recurrence of fever with nausea, headache, and joint pains which subsided within eight hours.

Procainamide was introduced in 1950 as a treatment for cardiac arrhythmias, and in the subsequent years it has become widely used because it has been effective and relatively nontoxic. It was developed as a substitute for a procaine which had previously been shown to have an antiarrhythmic myocardial action but had the undesirable properties of being short in duration of action and stimulatory to the central nervous system. Procainamide has rather rapid and complete gastrointestinal absorption and is slowly metabolized when compared with procaine. Untoward side-effects, such as anorexia, or nausea and vomiting, as well as a

tendency to sometimes produce a hypotensive state, are features of administration of this drug that are well known. Among the rather rare side-effects of administration of procainamide are ventricular fibrillation, ventricular tachycardia, and allergic reactions. Included in the allergic type of reactions thus far reported are rashes, asthma, and fever. Agranulocytosis, which has been reported, might also be an allergic reaction.

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THE FERTILITY TESTOR

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In previous issues of THE JOURNAL it has been demonstrated that the fertile period of the menstrual cycle can be concurrently identified by detecting a rise in the glucose content of the cervical mucous cascade utilizing Tes-Tape (paper impregnated with the enzyme, glucose oxidase) on either a swab [1] or a tampon.[2] Gluconic acid, the end-product, is converted to hydrogen peroxidase which, in the presence of traces of orthotolidine, produces a blue color that can be seen as shades of green when viewed on a yellow strip. The glucose present in the cervical mucus may be partly from aspirated liquor folliculi, but most of it is from glycolysis within the cervix itself.[3] A recent positive test from the cervix and cul-de-sac fluid of a patient who had previously undergone supracervical hysterectomy and bilateral salpingectomy without oophorectomy demands such a conclusion.

Both techniques required further improvement to minimize the contact of the Tes-Tape with glucose originating from the vagina itself. To this end we have successfully used a simple, inexpensive, permanent plastic syringe, like the Fertility Testor (see figure) designed by one of us. (F. J. E.). This consists of a narrow 6-in. hollow barrel perforated at its rounded tip by an orifice through which the strip of Tes-Tape may be thrust into contact with the cervix with the beveled nub of the plunger to which it has been affixed by a small plastic ring.

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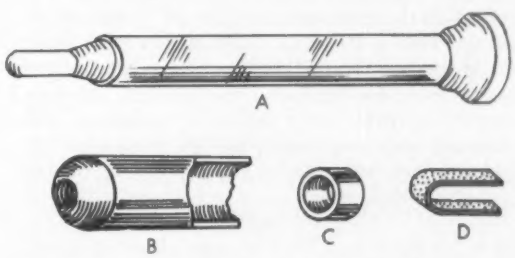
Method

It is preferable for the physician to introduce the syringe through a vaginal speculum in his office in order to acquaint the patient with the sensation of contact with the cervix. Care must be taken to introduce it into the vagina grasped like a pen, with the plunger inserted only halfway down the barrel, thus eliminating contact of the Tes-Tape strip with the vaginal secretions. Since at ovulation time the cervical mucus is a cascade 2 to 10 times its usual volume and is less viscid and more watery, the glucose-laden mucus bathes the posterior fornix



Fertility Testor. To use, (1) take apart by removing plunger, *A*, from barrel, *B*, then (2) remove ring, *C*, from tip of plunger, (3) measure strip of tape, *D*, from roll to cover entire narrowed tip of plunger, and (4) cover tip of plunger with strip of tape. (5) Hold tape in place by putting ring over tape and tip of plunger, push down ring until it fits snugly (no other fixative is required), and (6) replace plunger halfway into barrel.

of the vagina regardless of the direction of the external orifice of the cervix. After the barrel strikes the posterior fornix the plunger is gently pressed to force the tape through the opening at the tip of the barrel. After three minutes of deep cervical contact the patient is advised to withdraw the plunger and its affixed Tes-Tape through the barrel, thus avoiding contact of the tape with the vagina. Within three minutes after withdrawal the color of the Tes-Tape is compared with the blocks of three shades of green on the side of the Tes-Tape dispenser.

Interpretation.—Any color change appearing along even the sides of the Tes-Tape is significant, for by capillary attraction the glucose solution gravitates to the juncture with the dry Tes-Tape. If no sugar is present it remains yellow; a quantity less than 0.1% will result in pale green (+); and a quantity of glucose over 0.25% will produce a deep green (++) color. The color change is usually best seen in that portion of the Tes-Tape under the plastic ring. The deep green, indicative of a high glucose value, usually occurs synchronously with ovulation.[3] We find it useful to have the patient record her basal oral temperature on a chart each morning and the result of her glucose test below the temperature recording each evening prior to any coitus on every day of the cycle after the cessation of menstrual flow. If the patient must be up during the night, the temperature may be unreliable; but the glucose test is unaffected.

With such a concurrent indicator, the known variability of the relation of ovulation to the basal thermal shift—between two days before, the day of the thermal shift, and two days after it—can be more accurately checked. Actually, the appearance of a + result of the test, indicating a 0.1% glucose level, and the first ++ result, indicating a 0.25 level, usually precede the shift in basal temperature by a day or two. Occasionally the maximal glucose present does not exceed 0.1% (+), which is still significant and may represent the prevention of follicular fluid from reaching the cervix by neurogenic uterotubal spasm.[2]

Fertility Use.—The infertile couple will utilize for first coitus the day of the first + result, since sperm will survive until the day of the first ++ result. Usually the first ++ reaction occurs synchronously with rupture of the follicles as confirmed during culdotomy by simultaneous biopsies of the endometrium and the ovarian follicles or early corpora hemorrhagica (25 cases). A negative test result was seen on three other occasions when there was no ovulation. Similar accuracy of the Tes-Tape glucose reaction has been reported by Birnberg,[1] who obtained 20 successful therapeutic inseminations out of 27 attempts on the first day of the ++ reaction with a single insemination. Though small in numbers these reports suggest valuable consistency and utility of the test.

Its greatest usefulness appears to be for those patients with infertile husbands whose thermal shifts were prolonged, e. g., from day 7 to day 24. Prompt conception followed isolated coitus on day 11 when during the preceding month the glucose pattern was negative to day 9, followed by a + reaction on day 10, a ++ reaction on days 11 and 12, a + reaction on day 13, and negative through the rest of the cycle. An occasional patient may show a ++ reaction all month. However, if preceded by a hot-water douche and drying of the vagina by a tampon, more consistent readings may be obtained. For these patients, and for diabetics, the test may be of limited value. Naturally, use of this method can be no guarantee that pregnancy will or will not occur, since 25% of ova are abnormal and the conceptus does not necessarily nidate properly.

Use in Postponing Pregnancy—Concurrent Ovulation Rhythm Technique.—The highly fertile couple desiring for medical reasons to avoid pregnancy must be advised not to have coitus during the month until four days after the few days of positive glucose tests have ceased. Since one patient had positive glucose tests for four successive months on days 11 and 17, respectively, this test may aid those women who ovulate more than once a month to practice periodic continence (rhythm theory) more successfully by avoiding coitus until after any such secondary positive test.

Further confirmatory studies of the glucose content of the liquor folliculi [2] and tubal and uterine fluids and their relation to the fern pattern, sperm survival, and spinnbarkeit of cervical secretion are in progress.

Summary

An accurate calculation of fertility time can be made by simultaneous use of basal temperature charts and cervical glucose determinations made with use of an inexpensive permanent plastic syringe-like instrument, the "Fertility Testor," which permits the introduction of a strip of Tes-Tape (paper impregnated with the enzyme, glucose oxidase) for assay of glucose from the cervical mucous cascade at ovulation time, without interference from vaginal secretion.

520 Commonwealth Ave. (10) (Dr. Doyle).

The Fertility Testor is available on prescription only from physicians from the Fertility Testor Company, Ottawa, Ill.

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COMMITTEE ON MEDICOLEGAL PROBLEMS

CHEMICAL TESTING PROCEDURES FOR THE DETERMINATION OF ETHYL ALCOHOL

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This report is chapter 5 from a manual, being prepared by the Committee on Medicolegal Problems, dealing with medical and legal procedures involved in the use of chemical tests for intoxication.

Chemical analysis of the blood, urine, saliva, or breath gives the following information: first, it establishes the presence or absence of alcohol in the body; second, it determines the concentration in body fluids and tissues; third, it permits calculation of the approximate total quantity of alcohol in the body; and, finally, it furnishes the basis for calculation of the approximate volume of alcoholic liquor or beverage which may have been ingested within some hours prior to collection of the sample. Thus, chemical analysis not only furnishes objective data on the presence of alcohol in the body but also checks the reliability of statements with respect to ingestion of alcohol.

Observations on the subject's physical and mental state and the results of chemical tests together constitute the data on which judgment of the degree of intoxication is made.

Of the more than 200 analytical methods for ethyl alcohol, the majority have many common features with respect to such unit operations and unit processes as distillation, oxidation, and determination of the degree of oxidation. The majority depend on two important properties of alcohol: volatility and oxidizability. All methods, however, depend on one or more physical or chemical properties of alcohol, and all use one or more basic unit operations and unit processes for differentiation of alcohol from other compounds and for determination of ethanol identity and quantity. The differences between methods are largely in the combinations of the unit operations and in the details within each unit operation. The methods differ greatly in simplicity, speed, accuracy, specificity, sensitivity, and applicable range of concentrations. They therefore vary considerably in their adaptability to clinical and forensic problems.

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The existing methods, although large in number, fall into two categories: laboratory tests, applied principally to the analysis of blood, urine, and saliva; and on-the-spot tests, applied to the analysis of exhaled breath. Both categories of methods require not only understanding of the chemical principles but also skill in the chemical and instrumental manipulations. The laboratory should be well planned and organized; the equipment must be adequate; the analyst should possess training and experience at least equivalent to that of the clinical laboratory technologist, and preferably be a professional analytical chemist; and over-all supervision (or frequent consultation) should be maintained by an experienced toxicologist, clinical biochemist, or pathologist.

Basic Principles of Chemical Tests

All methods for the determination of ethyl alcohol in biological materials include several common elements: (1) sampling, including collection of exhaled air, body fluid, or other constituent, and measurement of the aliquot to be analyzed; (2) separation of ethyl alcohol from the biological material of the sample aliquot; and (3) quantitation of the separated alcohol. Some alcohol methods, particularly those for forensic application, include a fourth step: identification of ethyl alcohol and/or any possible chemically interfering substances as sample components.

Sampling.—Careful sampling, preservation, and handling are fundamental to accuracy. The identity and integrity of the sample must be maintained from the time of collection until analysis. This aspect of laboratory tests is far more exacting and difficult than that of on-the-spot tests, in which samples of exhaled breath are collected and immediately analyzed, but not stored. However, this feature of the laboratory tests not only permits many analyses by the same method in the same

laboratory, or redetermination by other methods, but also allows independent analysis in other laboratories.

Removal of Alcohol from Sample.—The techniques for removal of alcohol fall into three categories: diffusion-desiccation, aeration, and distillation. The latter includes simple distillation, steam distillation, and distillation under reduced pressure.

Diffusion-Desiccation.—The most widely known diffusion procedure is that of Widmark.[1] The sample is placed into a small glass cup which is suspended in a sealed flask containing oxidizing solution. In the Conway desiccation procedure, the apparatus consists of a covered cylindrical glass or porcelain dish with a center well. The sample is placed in the space surrounding the center well, which contains the oxidizing solution.

Aeration.—Aeration of the sample at room temperature and bubbling of the vapor through potassium dichromate and sulfuric acid solution or other oxidizing reagent has been used,[2] as has aeration at elevated temperatures, which shortens the required aeration time.[3]

Distillation.—Distillation of alcohol from the sample may be carried out with heat and evacuation or with steam.[4] The recovery of alcohol by these methods has not been as good as by simple distillation at atmospheric pressure; the apparatus for vacuum and steam distillation is more complicated, and the operation requires more attention and time. The recovery of alcohol by direct distillation at atmospheric pressure is quantitative, or nearly so; this procedure is therefore preferred.

Prevention of Foaming During Distillation.—Foaming is always encountered during distillation of untreated biological materials. It not only slows the rate of distillation but also may lead to considerable entrainment of impurities into the distillate. Precipitation of blood and tissue proteins eliminates foaming almost entirely.

Harger[5] precipitates the proteins by sodium tungstate and dilute sulfuric acid; an aliquot of the protein-free filtrate is then distilled. Trichloroacetic acid and other precipitants have been similarly used. Friedemann[6] has obtained an efficient precipitation by adding an acid mercuric sulfate–copper sulfate–ferric sulfate reagent to the sample, followed by adding calcium hydroxide suspension. The reagent removes sugars, primary and secondary amines, amino acids and proteins, sulfhydryl compounds, ketones, ketoacids, aldehydes, and many phenols. The filtrate from saliva may be analyzed directly without distillation.[6]

Direct distillation of the sample without previous precipitation of protein and filtration is preferred by most authors. The precipitant or antifoaming agent is added to the sample in the distilling flask. Picric acid is the oldest and perhaps most widely used antifoaming agent, but tartaric acid, both picric and tartaric acid, phosphoric acid, paraffin, mineral oil, and silicones have also been used.[7] The presence of high salt concentrations facilitates volatilization according to some analysts, who add large quantities of ammonium sulfate or sodium sulfate.

Tungstic acid and mercury salts are the most efficient precipitants and antifoaming agents, some analysts preferring the use of a combination of acid mercuric sulfate and tungstic acid, which permits rapid distillation of blood and urine samples without foaming.

Removing Interfering Substances from Distillates.—The most important volatile substances in forensic samples of blood and urine are organic acids, aldehydes, ketones, and phenolic compounds. Examples are formic, benzoic, and salicylic acids; formaldehyde and acetaldehyde (and paraldehyde, which readily decomposes to acetaldehyde when distilled with acid); acetone; and "carbolic acid" and menthol. The distillate may be treated with freshly precipitated silver oxide, which is added to the approximately neutral distillate and allowed to stand for some time before redistillation. For many years this has been a standard procedure for removing aldehydes and ketones. Silver oxide slowly oxidizes methyl and ethyl alcohols to the respective acids.

It has also been found that freshly precipitated mercuric oxide in approximately neutral solution efficiently removes aldehydes and ketones; during four or five hours' refluxing with the reagent, 3 to 5% of alcohol is lost. Greater quantities are lost at high alkali concentrations. Mercuric oxide has been similarly used. Some analysts recommend the addition of mercuric sulfate and an excess of calcium hydroxide suspension to the distillate. No loss of alcohol is noted at the approximately 0.08 *N* alkalinity of calcium hydroxide suspension.

Quantitative Determination of Separated Alcohol.—In all published alcohol methods quantitative determination of separated alcohol depends on one or more of the following analytical principles:

1. Isolation of ethyl alcohol and measurement of its mass or volume in pure form.

2. Determination of the physical properties of a distillate or vapor phase containing ethanol (e. g., by gas chromatography, interferometry, mass spectrometry, polarography, or measurement of specific gravity or refractive index.

3. Pyrogenic dehydration of ethanol to ethylene, followed by bromination, liberation of free iodine, and measurement of the latter.

4. Formation and estimation of iodine derivatives of ethanol (e. g., iodoform, ethyl iodide, etc.).

5. Conversion of ethanol to ethyl nitrate and measurement of hydrolysis of the latter by release of free iodine from potassium iodide.

6. Oxidation of ethanol to acetaldehyde and quantitation of the latter.

7. Enzymatic dehydrogenation of ethanol with alcohol dehydrogenase with simultaneous reduction of diphosphopyridine nucleotide (DPN) to dihydro-DPN, and measurement of the latter by ultraviolet spectrophotometry.

8. Oxidation of ethanol with a known standard oxidizing reagent to a predetermined color endpoint.

9. Oxidation of ethanol to acetic acid with an excess of oxidizing reagent and determination of the ethanol oxidized from the quantity of oxidizing reagent reduced as determined from the quantity of reaction products resulting, or by measurement of the excess of oxidizing agent remaining (by titration, photometry, spectrophotometry, visual color comparison, etc.).

10. Oxidation of ethanol to acetic acid and titration of the latter.

The last three procedures are employed most widely at present and therefore will be discussed briefly.

Oxidation of Isolated Alcohol: Choice of Oxidizing Agent.—Potassium permanganate, iodine pentoxide, and potassium dichromate are the most commonly used oxidizing agents.[8] Permanganate oxidation in acid solution is used in the Drunkometer on-the-spot test. Complete oxidation is accomplished rapidly. The reaction is sensitive, reproducible, and not noticeably affected by the small quantities of volatile substances other than alcohol which may be present in the exhaled breath of normal and intoxicated persons.

On the other hand, permanganate oxidation in alkaline solution is not specific for alcohol, yielding oxalic acid and carbon dioxide with alcohols, aldehydes, acetone, and other readily oxidizable substances. After alkaline oxidation, the solution may be acidified, which further oxidizes the oxalic acid to carbon dioxide. The residual permanganate is determined by various methods. The procedure is quite specific for alcohol if preceded by distillation from tungstate and acid mercuric sulfate and by redistillation from mercuric sulfate and lime, which removes (see above) most of the interfering classes of compounds.

Oxidation by iodine pentoxide has also been used.[9] The oxidation, which is carried out at high temperature, requires careful regulation and produces carbon dioxide and water. It is similarly complete for many other substances and therefore is not specific for alcohol. The oxidation is highly sensitive and reproducible. It is applicable only to determination of alcohol in vapors, and it is the basis for the Alcometer on-the-spot test for alcohol in breath.

The majority of methods employ oxidation by potassium dichromate in sulfuric acid solution. However, this oxidation has also been carried out in nitric acid and in phosphoric acid. The relative rates and the degree of oxidation of alcohol and other organic compounds (and therefore the specificity for ethyl alcohol) are affected by acid concentration and temperature.

At concentrations above 20 *N*, sulfuric acid (concentrated sulfuric acid has about 36 *N* titratable acid) dichromate yields acetic acid from ethyl alcohol, which is further oxidized to carbon dioxide and water. The greater the acidity the greater the rate, until, in concentrated acid, the complete oxidation to carbon dioxide is rapidly accomplished. Twelve oxidizing equivalents are used per mole of ethyl alcohol. In concentrated acid most other organic compounds are also oxidized quantitatively. Thus, the dichromate oxidation, although possessing maximal sensitivity, is nonspecific at high acid concentrations.

As the sulfuric acid concentration is decreased below 20 *N*, the interfering effect of many volatile substances like acetone, ether, and chloroform becomes negligible. Thus, ethyl alcohol is oxidized quantitatively to acetic acid by dichromate at 18 *N* acidity. The reaction has high specificity but is slower and only one-third as sensitive as in concentrated acid solution.

Oxidation of Isolated Alcohol: Colorimetry, Spectrophotometry, and Titrimetry.—The final step in all oxidative methods is a measurement by either chemical or instrumental means. In the majority of titrimetric methods the oxidation is carried out with excess dichromate, followed by determination of the residual dichromate by various methods. Some add potassium iodide and titrate the liberated iodine with standard sodium thiosulfate solution. Direct titration of the excess dichromate may also be done with potassium ferrocyanide in the presence of diphenylamine or with standard ferrous sulfate solution using such indicators as *o*-phenanthroline. The color of the reaction mixture after oxidation may be compared visually with known standards or measured photometrically.

In some of the earliest chemical methods, the volatile acidity was determined by distillation and subsequent titration by standard alkali. Aliphatic alcohols, such as ethyl alcohol, produce the respective fatty acids. Thus ethyl, propyl, and butyl alcohols produce acetic, propionic, and butyric acids respectively. Each of these acids has a characteristic rate of distillation. Each also has a characteristic distribution between water and various solvents. From the titration of total volatile acidity and the observed distribution, the respective alcohol may be identified and determined quantitatively.[10]

Sampling for Laboratory Tests

Choice of Specimen Materials.—The source, type, and quantity of specimen for alcohol determination depends on such practical considerations as availability of persons legally and technically qualified to obtain various types of samples, possible neces-

sity for procuring specimens in the field, available laboratory facilities, maximum time allowable for rendition of reports, and the desirability of minimizing the interval between the event in issue and the sampling time. Since alcoholic influence, in those states having statutory definitions, is expressed in terms of the concentration of ethyl alcohol in the blood, and since adequate correlations have been established between degrees of alcoholic influence and blood alcohol concentrations, it seems most direct and acceptable to analyze blood specimens, when possible. The blood alcohol concentration may be determined indirectly by analysis of any other body tissue or of exhaled air, using the known relations of distribution of alcohol between blood and tissues and between blood and alveolar air.

In practice, alcohol analyses are conducted on blood, breath, cerebrospinal fluid, saliva, tissues, and urine. When use of blood as a specimen material is impossible or undesirable, breath or urine specimens are most frequently employed for analysis, each having certain advantages and shortcomings. Thus, obtaining urine specimens from female subjects requires separate facilities and possibly, for forensic purposes, a female attendant able to identify the specimen as to its origin, noncontamination, or nondilution. Breath specimens are not readily collectible in duplicate or in sufficient quantity for later separate independent analyses by systems other than the Intoximeter (which makes such duplicate sampling a relatively expensive procedure) and generally must be analyzed immediately after collection in order to obtain reliable results. In dead persons, it may be difficult to obtain any specimen material, blood usually being the most readily and consistently available.

A number of technical problems must be considered in the use of blood specimens for routine alcohol determinations. During the early stage of alcohol absorption, the concentration of alcohol in arterial and venous blood may vary slightly. It has been suggested that only analysis of peripheral venous blood form the basis of precise interpretations; peripheral venous blood is probably also easiest to obtain in adequate quantities. Capillary blood, properly collected to avoid errors of sampling such as evaporation and dilution with tissue exudate, is also satisfactory, and the results of analysis approach those of arterial blood. Generally, the distribution or concentration of alcohol in the body fluids and tissues at equilibrium is in proportion to the water content.[11] The alcohol content of serum or plasma is about 10% higher than that of whole blood, in accordance with the water content of the body fluids. In any large-scale testing program occasional blood specimens are received which are partially clotted through use of ineffective anticoagulants or faulty sampling technique. Such clotted specimens can be analyzed without difficulty after homogenization.

Analysis of urine is used by many law enforcement agencies and clinical laboratories for the indirect determination of blood alcohol. Aside from the practical problem of collection facilities, two special technical considerations exist: the first is the relation between the level of alcohol in the venous blood and in the ureteral urine; the second is the relation between the alcohol content of the venous blood and of the urine present in the bladder at the time of collection of both, since any single random urine specimen represents a pooled ureteral urine sample, possibly further altered to some extent by alcohol diffusion through the bladder mucosa.[12]

Urine contains about 1.30 times as much alcohol as venous blood.[12] Most valid sampling systems recommend that the bladder be emptied and that one-half hour later the subject again be requested to void. The second sample is analyzed and the result, divided by 1.30, is taken as the concentration of alcohol in the venous blood at the time the test was made.[13] Our recommended routine is to collect two urine specimens at precisely known intervals of from 30 to 45 minutes after an initial complete emptying of the bladder, analyzing both later specimens in order to determine whether the subject's blood alcohol level, if any, was increasing or decreasing during the sampling period.

In estimating blood alcohol levels from urine analysis, one must realize that the levels in the first, second, and later specimens after initial emptying of the bladder represent an average of an infinite number of instantaneous ureteral urine alcohol levels during the entire secretion period of that specimen. Consequently, the blood alcohol level calculated by use of the distribution ratio of 1.30:1 is the blood alcohol concentration at a time midway between the beginning and the end of the collection period in the bladder and not the blood level at the time of voiding. All of these procedures assume that the bladder is emptied completely each time and that no residual urine is retained.

Postmortem Specimens.—In the collection of postmortem specimens, precautions must be taken to prevent contamination of the samples and to minimize changes of the alcohol level after their removal from the body. Enzymatic oxidation of alcohol to acetic acid can and does occur to some extent in the liver both before and after its removal from the body.[14] Alcohol can also be oxidized to acetaldehyde and acetic acid in vitro by brain, kidney, heart, and other tissues.[15] Since the oxidation is an enzymatic process, it can be minimized in vitro by effective refrigeration, preferably freezing at –20 C, which also tends to minimize putrefaction of tissue with attendant bacterial and fungal neoformation of alcohol and other volatile organic substances.[16] On the whole, these changes are small.

It is of considerable advantage to collect several different body materials in order to be able to estimate the stage of alcohol absorption existing at the time of death. Thus analyses of postmortem urine and blood yield considerably more information than either analysis alone. If the alcohol level in the urine exceeds that of the blood by more than 30%, assuming that both analytical results represent the actual levels at the time of death, it is obvious that a blood alcohol level existed at some time prior to death greater than either the urine or blood concentrations found post mortem and that the subject at the time of death was probably in the post-absorptive state with respect to the ingested alcohol. Conversely, if the postmortem blood alcohol level equals or exceeds that of the urine, the subject probably died in the absorptive phase and, therefore, probably within a few hours of the time of alcohol ingestion, which can frequently be fixed with some accuracy.[17] The possible import of such conclusions on explaining the cause, manner, and circumstances of death makes it advisable to collect two or more different body materials for postmortem alcohol determination.

The recommended routine is to collect adequate postmortem blood and bladder urine specimens whenever obtainable and to collect brain tissue and cerebrospinal fluid if those are available, as the next choice. Other tissues, such as liver and kidney, are less desirable but usable.

All postmortem body materials must be obtained prior to the start of any embalming procedure. Embalming fluids always contain considerable quantities of formaldehyde and methyl alcohol as well as other volatile substances, the presence of which in sample materials greatly complicates the analysis of ethyl alcohol; they may contain ethyl alcohol, which would render any postmortem alcohol analysis on embalmed tissues meaningless. Special precautions should be exercised against the frequent custom of collecting a postmortem blood specimen from the circulatory system effluent during arterial injection of embalming fluid.

The site of postmortem blood collection is of some importance, particularly in bodies which have been dead for some time, since it has been established that alcohol diffusion into the blood in the heart and the great vessels can occur from a large amount of alcohol in the stomach.[18] Because of the comparative ease with which adequate volumes of blood can be obtained, the heart and great vessels (aorta, pulmonary artery and vein, and vena cava) are the usual sites of collection, and uncontaminated specimens from these sources are satisfactory.[19] Adequate mixing of heart blood specimens before withdrawal is important; if it becomes necessary to withdraw heart blood from a body without autopsy, precautions against dilution of the blood with pleural or pericardial fluids should be employed. Adequate blood volumes for alcohol analysis can also be readily obtained post mortem from the femoral vein by raising the leg.

Size of Specimen.—With modern, sensitive analytical methods, smaller samples may be collected than formerly were required. Since alcohol is freely diffusible and is distributed in proportion to the water content, homogeneity of the sample is not a factor in the choice of sample size, as in the sampling of, say, food or coal for the determination of total nitrogen or calorie content. As reported by Freimuth and associates,[14b] there is no significant variation in alcohol concentration in different areas of the brain. The sample size is regulated by the quantities required for repeat determinations and for possible future rechecking of the analyses.

If necessary, 1 to 2 Gm. of tissue or 1 to 2 ml. of fluid can be analyzed readily. However, in practice, it is desirable to have larger quantities: 2 to 15 ml. of blood, cerebrospinal fluid, or saliva; 10 to 30 ml. of urine; and 10 to 50 Gm. of brain or other tissue. The sample should nearly fill the container.

Precautions During Collection.—Because of occasional claims in the literature that sterilization of the skin with alcohol can cause an apparent blood alcohol level of up to 0.25% w/w in abstaining subjects,[20] it is good practice to employ a non-alcoholic, nonvolatile skin antiseptic. Actually, controlled laboratory studies have consistently demonstrated that even excessive application of ethyl alcohol to the skin before venepuncture increases the existing blood alcohol level not more than 0.02%. Syringes and needles, of course, must be sterile, completely dry, and free of any trace of alcohol or other volatile substance. Consequently, alcohol, acetone, ether, or other volatile organic substances should not be used for sterilization or drying. Postmortem specimens should be collected with similar precautions except for sterility, and special care must be exercised to prevent contamination with any embalming fluid from needles, syringes, or containers.

Preservation.—From both the legal and analytical points of view, it is desirable to refrain as far as possible from adding preservatives or other substances to specimens. Tissue samples may be placed immediately after removal from the body into individual new, clean polyethylene freezer bags, which are sealed and placed into plastic-lined, cylindrical cardboard cartons and are then preserved solely by storage at –20 C in a deep-freeze refrigerator.[22] With this routine, we have found no change from the original alcohol content of brain tissue after 16 months. Freimuth and co-workers [14b] have demonstrated that storage of tissues in closed glass vessels at ordinary refrigerator temperature (5 C) does not prevent changes from the original

alcohol content; the brain alcohol level decreased from 0.22 to 0.12% and the liver alcohol level increased from 0.00 to 0.14% within 14 days.[18]

For preservation of blood specimens, from 0.1 to 1.0% of sodium fluoride (1 to 10 mg. per milliliter) is usually added to prevent glycolysis and other enzymatic changes; this is frequently combined with a supplementary anticoagulant, such as sodium citrate or potassium oxalate, in final concentrations of 0.3 to 0.5%. The following combination of anticoagulant and preservative, used in our laboratories (K. M. D.), preserves the original alcohol content of blood without change for at least 18 days at room temperature, for well over one month when combined with refrigeration at 5 C, and apparently indefinitely when combined with "deep-freeze" storage at –20 C: 150 mg. of sodium fluoride as preservative, plus 1 mg. of heparin sodium as anti-

TABLE 1.—*Alcohol Specimen Identification Form*

NAME OF LABORATORY
CITY AND STATE
See Reverse Side For Directions
PLEASE PRINT ALL INFORMATION

Subject's Rt. Thumb Print

SUBJECT: ..... (Last Name, First, Initial)
SUBJECT'S ADDRESS: .....
SPECIMEN: ..... (Nature, Sample Site)
SPECIMEN OBTAINED: ....:.....M....., 195.... by..... (Time, Date, Collector)
EXAMINE FOR: ☐ Ethyl Alcohol Content ☐ Other: .....
CHECK IF APPLICABLE: ☐ Container Unit seal was intact before use ☐ Non-alcoholic, non-volatile skin disinfectant ..... was user
REPORT RESULTS TO: .....
REMARKS: .....

FOR LABORATORY USE

CASE NO.: ..... SEAL NO.: .....
SUBMITTING AGENCY: .....
RECEIVED AT LABORATORY: ....:.....M....., 195.... (Time, Date)
FROM: .....
BY: .....

coagulant for up to 10 ml. of blood. These salts contained in 4 ml. of stock solution are deposited in film form on the container walls by drying in an oven at 95 to 100 C.[17]

Urine is readily preserved with 15 mg. of sodium fluoride per milliliter of urine, combined with refrigeration; with 3.5 mg. of benzoic acid per milliliter; or with 1 mg. of phenylmercuric nitrate per milliliter.

When specimen aliquots are measured by volume for analysis, the effect of the added substances on the original density of the sample can be neglected for all practical purposes, while such is not the case if the aliquots are to be weighed. Addition of the anticoagulants and preservatives in liquid form is obviously not permissible because of the resulting dilution of the original specimen. Sterile handling and storage of specimens, while desirable, is not necessary if the above directions are followed, particularly when combined with effective refrigeration.

Identity of Sample.—In forensic alcohol determinations, certain routine precautions are necessary to provide legally acceptable proof of specimen identity, integrity (absence of contamination or change from its original condition), and preservation of the chain of custody.[23] Identification of the specimen should be complete and definite, preferably by means of a numbered seal or similar device which simultaneously excludes tampering. Minimal information accompanying a specimen for alcohol determination, in addition to a concise statement of the test desired, should consist of the complete name of the subject from whom it was obtained; the nature of the specimen and site from which it was obtained (when applicable); the place, date, and exact time the specimen was obtained; and the name and other necessary particulars of the person obtaining the specimen.

An occasional problem in forensic analyses is the increasing tendency of courts to require positive affirmative proof of the identity of the subject from whom a disputed specimen was obtained, as well as of the identity of the specimen itself, during subsequent litigation, sometimes years later. We have recently placed the right thumbprint of the subject on the sample-identification record as a precaution against such difficulties. A suggested form for identification of specimens is shown in tables 1 and 2. The form has been in use several years in the laboratory of one of us (K. M. D.).

Analytical Significance of Test Results

Correct interpretation of the analysis in terms of actually existing alcohol concentrations at the sampling time is basic to valid physiological evaluation of alcohol test results. Such analytical interpretation of the results of an alcohol analysis is subject to certain purely technical and scientific considerations unrelated to physiological aspects.

The statutory definitions of alcoholic influence or intoxication promulgated in the United States, and expert testimony concerning the same, uniformly express blood and other body material alcohol concentrations in terms of weight/weight per cent. It is, however, universal practice in the United States to perform practically all clinical chemical analyses upon volumetrically measured specimen aliquots. Such volumetric measurement is desirable for technical reasons, such as the change from original density of a specimen material caused by preservatives, and for the expediency of greater speed with adequate precision. If, however, in interpreting the reported tissue or fluid alcohol levels the deviation from weight/weight percentage is not known or considered, significant misinterpretations can occur. Blood, for example, has an average specific gravity of 1.055 and can have an even greater density if the cell volume is unusually high. Thus a blood alcohol level of 0.152 weight/volume per cent (i. e., 1.52 mg. per milliliter) is equal to a level of only 0.144 weight/weight per cent (i. e., 1.44 mg.

per gram). Reported to two decimal places and without specification these values become, respectively, "0.15%" and "0.14%." A hairline legal interpretation made without awareness of the difference caused by the volumetric sampling could conceivably result in a decision different from that which would have resulted from a report on the weight/weight basis, even though the difference is physiologically negligible. The remedy lies in factual reporting of blood and other alcohol concentrations in terms of the actual measurement employed, accompanied either by an estimated recalculation to any other measurement system of interest or, better, by an explanation of the deviation limits attributable to the difference in measuring technique.

Alcohol determination results should include a statement of the precision limits attached to the measurement. This may be done by reporting a given alcohol level to the first doubtful figure and adding the precision limits (e. g., $0.196 \pm 0.004\%$ w/w). Reporting only two significant figures (e. g., 0.19% w/w) is preferable, since it is more meaningful physiologically, and is recommended practice. Few, if any, practical alcohol determination methods have a precision greater than 3 to 5% of the alcohol actually present, and reporting of the third significant figure is entirely unwarranted in the physiologically possible concentration range (0.00 to about 0.70% w/w). In expressing the results quantitatively at all, the analyst implies that the report refers to a single determined substance, universally understood to be ethyl alcohol. The validity of such implication depends on the relative specificity for ethyl alcohol of the particular method employed. It is, consequently, good analytical practice and legally desirable to establish experimentally by qualitative tests, to a reasonable degree of certainty, the presence of ethanol and the absence of any substances which could react like ethanol in the analytical system used.

The concordance between a reported true ethyl alcohol level and the original alcohol level in the sample material at the time the sample was obtained is not under the control of the person making a physiological evaluation of an analysis result. The concentration of ethyl alcohol found in body fluids and tissues is a function of the following factors: (1) concentration of alcohol actually present originally; (2) percentage of recovery of actually present alcohol, a characteristic of the individual analytical method; (3) loss of alcohol originally present, after removal of the specimens from the body, from such causes as enzymatic oxidation, and evaporation; and (4) postremoval gain in alcohol as the result of neoformation, by enzymatic fermentation or other factors. In addition, there is the problem of false apparent alcohol concentrations yielded by nonspecific analytical methods, in the presence of various concentrations of volatile reducing bodies produced by decomposition and putrefaction of biological materials, such as aldehydes, amines, ketones, phenols, and sulfides.

It is apparent that during prolonged intervals between the removal of tissues or fluids for alcohol determination and the analysis, particularly in inadequately preserved specimens, the various factors can operate jointly to reduce or obliterate a low original alcohol level, to reproduce accidentally by loss and neoformation the original concentration, or to produce a significant true or apparent alcohol concentration in an originally alcohol-free specimen. The analyst should make every reasonable effort to preserve the specimen until analyzed in as nearly as possible the original state in which it was received by him; and he should indicate in his report factors which might lead to alteration of any original alcohol concentration, such as evidence of sample decomposition or unusual or unidentified specimen odor.

Appendix A presents the details of four laboratory procedures for analysis of tissue and body liquids for ethyl alcohol.

TABLE 2.—*Reverse of Specimen Identification Form*

DIRECTIONS FOR COLLECTION AND SUBMISSION OF SAMPLE

1. This bottle contains sodium fluoride as a preservative and sodium heparin as an anticoagulant; and is suitable for submission of blood, urine, cerebrospinal fluid or other liquid specimens. Do not add anything other than the sample to the container.
2. Use only a sterile, dry, clean syringe and needle for obtaining specimens and, where necessary, use only a non-alcoholic, non-volatile skin disinfectant. Place approximately 10 ml. of whole blood or other liquid specimen into the bottle, cap tightly, and gently shake about 1 minute to dissolve the chemicals.
3. Replace the specimen bottle and this completed form into container; then seal cap with the wire and numbered seal furnished. If possible, refrigerate entire container until mailed or delivered to the laboratory.
4. The specimen in its sealed container may be delivered to the laboratory by messenger or sent by U. S. Mail, preferably by "CERTIFIED MAIL—RETURN RECEIPT REQUESTED."

On-the-Spot Tests

Characteristics and Application.—The great majority of alcohol determinations on human body materials are performed in connection with the investigation of alleged traffic offenses, chiefly on motor vehicle operators suspected of driving while under the influence of alcohol. While theoretically analysis of any body fluid would suffice for the direct or indirect determination of the blood alcohol concentration at the time of the offense, the indirect determination of the blood alcohol level by breath alcohol analysis has proved to have certain special advantages in these situations.

Inherently, in traffic law enforcement and in a few other special situations (differential diagnosis of intoxication states, particularly in persons in police custody; assessment of fitness for specialized tasks like aircraft piloting, railroading, and industrial operations), it is desirable to obtain immediate information concerning the subject's approximate blood alcohol concentration at the time of the investigation, in order to provide a sound basis for instant corrective or other actions which in many cases have far-reaching effects (e. g., arrest, suspension from employment). Conventional methods

for alcohol analysis in body liquids (blood, urine, saliva, etc.) require relatively elaborate laboratory facilities frequently not in operation or otherwise unavailable at the time these problems arise, and they usually require longer to perform than it is practical to wait for decisions based on the analysis results. Geographical inaccessibility of such laboratory facilities or even of personnel qualified to obtain blood specimens is a frequent factor in traffic law enforcement, particularly in county and state highway patrol operations.

To provide on-the-spot alcohol analyses of the required reliability and practicability, a number of rapid field procedures have been developed. In practice, because of the requirements for minimal physical facilities and technical proficiency, such on-the-spot techniques are limited to breath alcohol analysis. These breath alcohol analyses all share the following characteristic advantages:

1. A breath alcohol analysis result, usually expressed in terms of the blood alcohol concentration, is obtained within a few minutes.

2. Breath as the analyzed material accurately reflects the actual blood alcohol level at the time of the test, without lag or overrun, and is often obtainable nearer the time in issue than other materials.

3. When breath obtained at the time of the analysis is used as the specimen, the problem of positively identifying the specimen donor is eliminated, as are most of the collection, identification, preservation, transportation, and evidentiary safeguard problems common to other body materials, together with the need for specially qualified collection personnel, for special collection facilities and containers, and for most of the precautions outlined in detail in the section entitled "Sampling for Laboratory Tests."

4. Since breath analysis eliminates certain difficult steps of the tissue and liquid alcohol analyses, requirements for technical background and skill of the analyst are greatly reduced.

5. Required test facilities can be minimal and are usually limited to the self-contained breath alcohol apparatus used, costs per test after acquisition of the necessary equipment being generally much lower than for comparable laboratory analysis.

6. There is frequently less objection by the tested subject to collection of a breath sample for alcohol analysis than to the body penetration required to obtain a blood specimen, and generally less cooperation and considerably less time are required than for collection of adequate saliva or urine specimens. The embarrassment connected with obtaining a urine specimen under observation is avoided.

7. Multiple, replicate, and serial alcohol determinations at frequent brief intervals are practical, because of the rapidity and relative simplicity of on-the-spot analyses and the rapid nontraumatic sampling of breath specimens, allowing accurate determination of the directional trend of the blood alcohol curve and many experimental analyses on a given subject.

On-the-spot breath analyses also embody a few inherent limitations:

1. Entire breath specimens cannot be effectively preserved for later replicate or independent confirmatory analysis, although the alcohol from a measured volume of breath can be collected and preserved for later analysis.

2. Some cooperation is required from the patient for collection of an adequate breath specimen, the extent varying with the nature of the required breath sample (alveolar air, mixed expired air, or rebreathed air) and the collection apparatus (balloon, sample chamber of apparatus, etc.).

3. Most breath alcohol methods, except, under some conditions, those employing the alcohol–carbon dioxide ratio, are inapplicable to unconscious or completely uncooperative subjects.

4. A period of approximately 10 to 15 minutes after the last ingestion of alcohol (or regurgitation) must elapse before breath alcohol analysis, to insure elimination of the possible effects of any residual mouth alcohol.

These characteristics of the on-the-spot alcohol tests make them highly useful as rapid and simple screening tests to indicate or obviate the need for confirmatory body fluid alcohol determination, such as blood alcohol determination, and to furnish approximate blood alcohol level data. Under properly controlled conditions, which include proper training and continuing expert supervision of competent operators and adequate expert control of equipment, reagents, and procedures, the on-the-spot tests are also capable of yielding accurate breath alcohol concentration results, acceptable as an index of blood alcohol concentration of adequate reliability for clinical and legal purposes.[25] The significant human physiological characteristics (blood composition, body temperature, respiratory action, etc.) normally vary within sufficiently narrow limits to permit full realization of this technical potential.[26]

General Principles.—Since the first application of breath alcohol analysis to medical purposes in the United States by Bogen in 1927, a number of breath alcohol analysis methods and devices have been developed. They fall into three functional categories: (1) laboratory alcohol determinations, performed on laboratory-collected breath specimens, or on those collected in the field with on-the-spot breath screening-and-collecting equipment, yielding definitive blood alcohol level results; (2) field (on-the-spot) breath alcohol determinations employing portable apparatus and yielding definitive blood alcohol level results; and (3) semiquantitative field (on-the-spot) breath alcohol screening tests employing portable apparatus or disposable single-test units, yielding only approximate blood alcohol level results.

All breath alcohol analyses depend on the fundamental principle that the distribution of alcohol between circulating pulmonary blood and alveolar air occurs by simple diffusion and, like that of other volatile substances, obeys Henry's law, meaning that distribution equilibrium exists and that consequently for a given temperature a constant ratio exists between the concentrations of alcohol in the blood and in alveolar air. (Henry's law is as follows: The mass of gas dissolved by a given volume of solvent, at constant temperature, is proportional to the pressure of the gas with which it is in equilibrium, whence concentration of gas in liquid phase÷concentration of gas in gaseous phase=constant at a definite temperature.)

There is general agreement that the mean value of this Ostwald partition ratio of blood alcohol concentration to alveolar air alcohol concentration at the average temperature of exhaled air (34 C) is approximately 2,100:1; i. e., 2,100 ml. of alveolar air contain the same quantity of alcohol as 1 ml. of blood.[27] The breath alcohol methods determine the quantity of alcohol in a known volume of breath or measure the breath volume required to furnish a known quantity of alcohol, in either case yielding a breath alcohol concentration, generally expressed in milligrams of alcohol per liter of breath. From the blood alcohol–alveolar air alcohol ratio of 2,100:1 and knowledge of the alveolar air content of the analyzed breath sample, the corresponding blood alcohol level is then readily calculated. Alcohol quantitation is accomplished by the same general chemical principles outlined under "Basic Principles of Chemical Tests," above, usually controlled oxidation with iodine pentoxide, potassium dichromate in acid solution, or potassium permanganate in acid solution.

A key element in each breath alcohol method is the procedure employed for determination of the quantity of alveolar air actually analyzed for its alcohol content, the following methods being employed:

1. Alveolar air is collected, as by mechanically trapping the final portion of a prolonged expiration (volume greater than 400 ml.), and analyzed directly.

2. Rebreathed ("venous") air, which is identical in alcohol concentration to alveolar air, is obtained by having the subject rebreathe ordinary expired air four or five times with the nostrils closed and is analyzed directly.

3. Mixed expired air is collected and analyzed for alcohol and carbon dioxide content. The proportion of alveolar air in the sample is estimated from its carbon dioxide concentration on the basis of observations that the alveolar air of normal individuals contains about 5.5% carbon dioxide by volume, while atmospheric air contains only approximately 0.03 vol. % carbon dioxide.

4. Mixed expired air is collected and analyzed for alcohol only. As screening methods for the estimation of the approximate blood alcohol level, some "volumetric" tests assume that ordinary expired breath normally contains about 58 to 63% alveolar air and hence employ an equivalence factor of approximately 3,200 ml. of ordinary mixed expired breath measured at 25 C as containing the same quantity of alcohol as 1 ml. of blood.

Reliability.—Correlation Between Blood Alcohol Levels Obtained by Direct Blood Analysis and from Breath Analysis: The validity of breath alcohol analysis for the determination of the blood alcohol level depends on two components: the analytical reliability of the breath alcohol analysis itself and the constancy to the required extent of the human physiological variables affecting the formulas for conversion of the breath alcohol concentration to blood alcohol concentration. Both factors are tested by examining the closeness with which breath alcohol analyses predict actual blood alcohol levels. Consequently, the correlation between breath analysis–derived blood alcohol levels and those obtained by direct blood analysis has been universally employed as a measure of the reliability of breath alcohol analyses for the indirect determination of blood alcohol concentrations and has been extensively studied.

In evaluating such studies, the physiological and technical variables inherent in blood alcohol analysis as well as those attending breath alcohol analysis must be recognized and considered. Analytically, the blood alcohol methods are subject to considerable variation in reliability, with the chemical accuracy, precision, and specificity of some methods for the determination of blood alcohol being far inferior to those of reliable methods for the determination of breath alcohol. Consequently, the significant reliability characteristics of the referee blood alcohol method must be known and considered in comparing the results of simultaneous blood and breath alcohol analyses. Any substantial difference in collection times of the blood and breath specimens should also be considered, particularly in the light of the usual experimental conditions which sometimes preclude complete alcohol distribution equilibrium. These external variables, of course, are absent in correlation studies of the results of simultaneous breath alcohol analyses by different systems or instruments.

Carefully controlled experimental studies of the more commonly employed breath alcohol methods have been conducted recently, employing adequately reliable referee blood and urine alcohol methods and models of the Alcometer, Breathalyzer, Drunkometer, and Intoximeter in current production at the time of the respective tests. These recent studies uniformly and conclusively demonstrate that breath alcohol analysis performed by competent operators under expert supervision with properly controlled apparatus, reagents, and procedures can justifiably

be expected consistently to yield by calculation blood alcohol concentration results within 0.015 weight per cent ethanol of those obtained by direct analysis of blood. The same deviation limits can usually be expected between calculated blood alcohol levels from simultaneous breath analyses by two or more different breath alcohol methods.

Specificity: The specificity of on-the-spot breath alcohol analysis methods is an important consideration, since the nature of most of these tests precludes analytically establishing the absence of interferents; that is, volatile reducing substances which like ethyl alcohol diffuse from the blood into the alveolar air and some of which can reduce the commonly employed oxidizing reagents.

The major reagents employed for alcohol quantitation in breath are iodine pentoxide, potassium dichromate in sulfuric acid solution, and potassium permanganate in sulfuric acid. Of these, iodine pentoxide is the least selective reagent for ethanol, since it readily oxidizes many organic substances, including aldehydes, carbon monoxide, ethyl ether, various hydrocarbons, ketones, and methyl alcohol. Potassium dichromate in acid solution is known to react with aldehydes, ether, methyl alcohol, etc. In general, low concentrations of acetone cause no interference under the reaction conditions employed in breath tests, and food-derived odoriferous flavor substances cause none. Potassium permanganate in approximately 15 *N* sulfuric acid at room temperature, as used in breath alcohol analysis, is probably the test reagent most selective for ethanol, being unaffected by acetone and many volatile food-derived substances in the low concentrations found in breath (citrus fruit oils, cheeses, garlic, onions, etc.), although it reacts with acetaldehyde. Only iodine pentoxide is significantly affected by tobacco smoke, which in practical breath test operation, of course, is totally excluded.

The general alcohol specificity and characteristics of the several reagents are further modified by other variables of the individual breath alcohol methods, such as breath volume analyzed and reaction temperature. Consequently, each breath alcohol method must be evaluated as a whole in regard to its freedom from chemical interference. The entire interference problem is somewhat academic, because in the conditions under which breath tests are employed, predominantly in traffic law enforcement, substances chemically capable of interfering are generally not present in concentrations yielding markedly false apparent alcohol levels. Conversely, the possible presence of food odors, halitosis, and similar conditions will not prevent complete reaction of alcohol with the breath test reagents, nor will masking of beverage odors on the breath, as by chlorophyllin, affect the alcohol content of the breath or the breath alcohol tests.

TABLE 3.—*Comparison of Current Major on-the-Spot Breath Alcohol Test Methods*

Apparatus Employed	Method: Developer(s)	Method: Yr. Published	Material Analyzed	Alcohol Equivalent of 1 Ml. of Blood	Reagent Used for Alcohol Quantitation	Test Category	Approximate Cost of Apparatus
Alcometer	Greenberg and Keator	1941	Alveolar breath, 12 ml.	2,100 ml.	Iodine pentoxide	Quantitative breath analysis	$700 +0.38/test
Alcotest	Grosskopf and Scheibe	1953	Mixed expired breath, 1,000 ml.	2,300 ml. at 34 C	Potassium dichromate in sulfuric acid	Preliminary screening test	$0.75/test
Breathalyzer	Borkenstein	1954	Alveolar breath, 52.5 ml.	2,100 ml.	Potassium dichromate in sulfuric acid	Quantitative breath analysis	$595 +0.60/test
Drunkometer	Harger and co-workers	1938	Mixed expired breath, volume varies	Alcohol-CO_2 ratio: 190 mg. CO_2	Potassium permanganate in sulfuric acid	Quantitative breath analysis	$225 +0.60/test
		1938	Mixed expired breath, volume varies	3,200 ml., CO_2-free, at 25 C	Potassium permanganate in sulfuric acid	Preliminary screening test	Included with above
		1956	Rebreathed air, volume varies	2,100 ml.	Potassium permanganate in sulfuric acid	Quantitative breath analysis	$225 +0.60/test
Drunkotester	Kitagawa and Kobayashi	1953	Mixed expired breath, 100 ml.	3,300 ml. at 25 C	Potassium dichromate in sulfuric acid	Preliminary screening test	$21.50 +0.20/test
Intoximeter	Forrester and co-workers	1941	Mixed expired breath, volume varies	Alcohol-CO_2 ratio: 190 mg. CO_2	Laboratory analysis	Breath collection unit for laboratory quantitative analysis	$4.25 for collecting unit
		1941	Mixed expired breath, volume varies	2,800 ml. at 34 C	Potassium permanganate in sulfuric acid	Preliminary screening test	Included with above

True reactions with alcohol in expired breath from sources other than the alveolar air (eructation, regurgitation, vomiting) will, of course, vitiate the breath alcohol results but can be detected by observation of the test subject and prevented by the subject's rinsing out his mouth with water.

The rapidity and simplicity of the breath alcohol tests and the individual differences in sensitivity to nonalcohol reducing substances actually lend themselves to a unique application as a semiautomatic qualitative chemical identification system differentiating ethyl alcohol from other reducing substances: Substantially identical alcohol level results (two or more results agreeing within 0.015% w/w) obtained by two different chemical reaction principles (e. g., iodine pentoxide and potassium permanganate oxidations) offer chemical proof of the reducing substance measured being ethyl alcohol, as well as reasonably conclusive evidence of the proper functioning of each test. Presence of a significant concentration of nonalcoholic reducing

substance in the breath (with or without presence of ethanol) would affect the different chemical trains in a nonidentical manner and to different degrees and would, therefore, yield quantitatively different apparent "ethyl alcohol" results. For example, presence of much acetone in the breath would cause substantial apparent "alcohol" level results in instruments employing the iodine pentoxide reaction but would not affect breath alcohol methods utilizing potassium permanganate in acid solution.

Calibration and Testing of Apparatus.—The several commercial breath alcohol apparatus either incorporate instrument scales reading directly in blood alcohol concentration or provide calibration tables yielding blood alcohol levels from the observed variables (breath volume analyzed, weight of carbon dioxide absorbed, etc.). The accuracy of blood alcohol concentration predictions by these means can, of course, be checked by direct analysis of a simultaneously obtained blood sample, keeping in mind the referee method limitations.

Simpler methods and apparatus have, however, been developed for calibration and testing of breath alcohol determination instruments, employing mixtures of ethyl alcohol in air or other gases. Careful experimental work has established considerable independently confirmed data on the partition ratio of alcohol between air and water at various temperatures. Using this information, one can easily prepare various known concentrations of alcohol in air by equilibrating air with aqueous alcohol solutions of known concentration. A simple equilibrator consists essentially of a closed metal, glass, or plastic cylinder bearing an air inlet tube terminating in a porous gas-dispersion disk or cylinder, a thermometer, and an air outlet tube connected to a liquid trap. Room air is forced through a 5-cm. layer of alcohol solution by means of an atomizer bulb, in a flow of very small air bubbles, thus attaining complete alcohol distribution equilibrium in one passage; the resulting alcohol concentration of the effluent air is controlled by the concentration of alcohol in the solution and by the temperature.

Analysis of an adequate number of such known air-alcohol mixtures in a breath alcohol apparatus will yield the necessary information for preparation of calibration scales or calibration tables. The original and continuing validity of these or of factory precalibrations can be readily confirmed whenever desired by analysis of one or more air alcohol samples.

EXAMPLE OF CALIBRATION CHECK:

1. The mean alcohol partition ratio constant for the air-water system, $k_{A/W}$, is 0.000217 at 25.0 C. (Ostwald partition ratio coefficient, $k_{A/W}$=weight of alcohol per unit volume of air÷weight of alcohol per unit volume of water.) Hence, 1 liter of air equilibrated at 25 C with water containing 4 mg. of ethanol per milliliter will contain $(1{,}000 \times 4 \times 0.000217) = 0.868$ mg. of alcohol.

2. 2,100 ml. of this air, warmed to 34 C, will contain

$$\left[2.1 \times \frac{(273 + 25)^\circ}{(273 + 34)^\circ} \times 0.868 = \right] 1.769 \text{ mg. of alcohol.}$$

3. A person whose alveolar air contains the same alcohol concentration, 1.769 mg./2,100 ml., will have a blood alcohol level of (1.76 mg./ml.)=0.17% w/v, according to the established blood–alveolar air partition ratio of 2,100:1 at 34 C.

4. Analysis of the above air-alcohol mixture in a breath alcohol apparatus should, therefore, yield the theoretical blood alcohol concentration reading of 0.17% w/v, or (0.17/1.055)=0.16% w/w.

Breath Alcohol Tests

Methods for breath alcohol analysis have been used for many years. The principles and techniques of practical breath alcohol testing as an on-the-spot method will be illustrated by describing briefly in appendix B the components and operation of the six presently commercially available breath alcohol instruments: the Alcometer, the Alcotest, the Breathalyzer, the Drunkometer, the Drunkotester, and the Intoximeter. Some characteristics of each apparatus and of the methods developed for its use are shown in table 3.

Appendix A

LABORATORY PROCEDURES FOR ANALYSIS OF TISSUES AND BODY LIQUIDS FOR ETHYL ALCOHOL

Four methods for the determination of ethyl alcohol in biological materials, all presently well known and widely used in the United States, will be described as exemplifying the many published procedures. Their selection for discussion here does not imply any inferiority of any other procedure. The methods described are equally applicable to tissues, blood, urine, and other body fluids, with some slight modifications for each type of body material. For example, tissues require initial preparation by grinding, blending, or fine comminution to assure homogeneity. Tissue homogenates and blood may be treated by preliminary precipitation of proteins, or they may be distilled directly with the addition of protein precipitants to the distillation flask. The methods described have several common characteristics: all employ distillation for separation of the ethyl alcohol from the specimen; the alcohol in the distillate is quantitated in each by oxidation, using potassium dichromate in sulfuric

acid solution below the critical concentration of 20 *N*, the oxidations, in fact, being carried out at less than 18 *N* acidity. Under these conditions, ethyl alcohol in the distillate is quantitatively oxidized to acetic acid and volatile impurities exert minimal interference.

The differences between the methods are in (*a*) the method of distillation, whether by direct distillation or distillation of a deproteinized filtrate; (*b*) the choice of protein precipitants; (*c*) the size, type, and construction of the distillation apparatus; (*d*) the sulfuric acid concentration (ranging from about 17 *N* to 2 *N*) and the potassium dichromate concentration used during the oxidation, with consequent differences in the range of alcohol concentration of the several methods; and (*e*) the measurement of changes in the oxidizing reagent, whether by visual colorimetry, spectrophotometry, or titrimetry. The last represents the most important and distinctive difference between these methods.

Heise Method

The Heise method [7] is as follows:

Principle.—The specimen, commonly blood or urine, is distilled directly from a mixture of picric and tartaric acids to precipitate the proteins and reduce foaming. Varying volumes of distillate in a series of test tubes are made to a constant volume with distilled water. A measured volume of potassium dichromate in sulfuric acid is added and the resulting mixture, at 7 to 8 *N* acidity, is heated in a boiling water bath. The resulting colors are compared visually against a series of 21 color standards prepared with known quantities of ethyl alcohol.

TABLE 4.—*Strong Permanent Standards*

Nominal % Alcohol	Alcohol by Weight	Water, Ml.
0.00	0.00 ml.	1.00
0.00	0.50 ml. of 0.10% by weight	0.50
0.10	1.00 ml. of 0.10% by weight	0.00
0.12	0.60 ml. of 0.20% by weight	0.40
0.14	0.70 ml. of 0.20% by weight	0.30
0.16	0.80 ml. of 0.20% by weight	0.20
0.18	0.90 ml. of 0.20% by weight	0.10
0.20	1.00 ml. of 0.20% by weight	0.00
0.22	0.73 ml. of 0.30% by weight	0.27

Apparatus

1. Distilling apparatus: 500-ml. distilling flask and small condenser. (Equipment and reagents for this procedure are available from LaMotte Chemical Products Co., Towson, Baltimore 4, Md.)

2. Pipets, volumetric.

3. Water bath.

Reagents.—All reagents for this and all following procedures are prepared with analytical reagent grade, chemically pure (C. P.) reagents and distilled water free of reducing substances as shown by suitable purity tests.

1. Oxidizing reagent: 0.33% potassium dichromate in 50% sulfuric acid by volume.

2. Protein precipitants: half-saturated picric acid solution, containing 10% tartaric acid.

Procedure A: Urine Analysis

1. Slowly distill a mixture of 10 ml. of urine and about 10 ml. of picric–tartaric acid protein precipitant from a 500-ml. Florence flask, collecting the first 10 ml. of distillate.

2. Into separate test tubes similar to those used for the standards, place 1 ml. and progressively smaller measured volumes of distillate, making the volume up to 1 ml. in each case with distilled water. Add 3 ml. of the oxidizing reagent to each tube; mix, stopper, and place the tubes in a boiling water bath for four minutes.

3. Cool test tubes and visually compare the resulting colors by transmitted light against the "strong permanent standards" prepared as described in table 4. Divide the nominal alcohol concentration of the matching standard tube by the fraction of 1 ml. of distillate oxidized, to obtain the alcohol percentage of the original urine specimen.

4. If the results are too low to be read, use the weak standards and follow steps 2 and 3 of procedure B below, in which event the alcohol percentage of the original urine specimen=[nominal alcohol concentration of standard ÷ volume of distillate used (milliliters)]×2.

Procedure B: Blood Analysis

1. Add 2 ml. of whole blood to about 15 ml. of the picric–tartaric acid protein precipitant. Distill slowly and collect the first 10 ml. of distillate.

2. Into separate test tubes similar to those used for the standards, place 2 ml. and smaller measured volumes of distillate, making the volume up to 2 ml. in each case with distilled water. Add 1 ml. of the oxidizing reagent to each tube; mix, stopper, and place in a boiling water bath for 12 minutes.

3. Cool the test tubes and visually compare the colors against those of the "weak permanent standards" prepared as described in table 5. Multiply the nominal alcohol concentration of the matching standard tube by [10 ÷ volume of distillate used (milliliters)] to obtain the alcohol percentage of the original blood specimen.

Preparation of Standards

1. Strong Permanent Standards: To each of nine test tubes of uniform diameter add the volumes of alcohol solution and of distilled water indicated in table 4. Add to each tube 3 ml. of oxidizing reagent; stopper the tubes, place in boiling water for four minutes, cool, and seal.

2. Weak Permanent Standards: To each of 12 test tubes of uniform diameter add the volumes of alcohol solution and of distilled water indicated in table 5. Add to each tube 1 ml. of oxidizing reagent; stopper the tubes, place in a boiling bath for 12 minutes, cool, and seal.

Critique.—This is the simplest of the four procedures described, requiring relatively little laboratory space and no special glassware or appa-

ratus. The alcohol recovery of the method as originally described by the author is not as accurate or constant as in the other three methods which follow, chiefly because of the large capacity of the apparatus compared to the small volume of liquid. The distillation is tedious, and much foaming may be encountered with blood samples. The color standard provide steps in color changes (not a continuous series) to which the unknown is approximated. The method thus incorporates both systematic errors and a small, variable, subjective error. Recoveries of 91 to 112% of added alcohol by this method have been reported. A single analysis requires about 20 minutes. Acetone, chloroform, and ether do not interfere in this method.

However, the accuracy and speed of the procedure approaches that of the other methods which will be described, provided the all-glass distillation apparatus and the antifoam agents or precipitants of those methods are used.

Dubowski Method

The Dubowski method [4] is as follows:

Principle.—Specimens of any body fluid (or steam distillates of tissue homogenates) are distilled directly from tungstic acid to precipitate the proteins. An aliquot of the distillate is mixed with a measured volume of standard potassium dichromate in sulfuric acid and the resulting mixture, at 15 *N* acidity, is oxidized at 100 C. The residual potassium dichromate is measured spectrophotometrically at 450-mμ wave length and the corresponding alcohol concentration of the original specimen is obtained from a calibration curve or table prepared from analysis of solutions of known alcohol content.

Apparatus

1. Distilling apparatus: Direct and steam distillation apparatus of Dubowski and Shupe [27] (catalog number SB-1715X, Scientific Glass Apparatus Co., Inc., Bloomfield, N. J.) or distillation apparatus of Harger (see below).

2. Fluid bath: Electric water bath at 100 C or electric constant temperature bath at 100 C, with permanent water-soluble bath fluid (UCON fluid 50-HB-280X, Carbide & Carbon Chemicals Co., 30 E. 42nd St., New York 17, N. Y.).

3. Photometer: Beckman model DU or model B spectrophotometers; Bausch and Lomb Spectronic-20 spectrophotometer; Coleman model 14, 6B, 6C, or 6D spectrophotometers; or filter photometer with microcuvettes and blue filter transmitting in the region of about 450 mμ.

4. Volumetric ware: good grade of pipets and glass-stoppered volumetric flasks.

Reagents

1. Oxidizing reagent: 0.0214 *N* potassium dichromate; 1.0500 Gm. $K_2Cr_2O_7$ in 1 liter of 50 vol. % sulfuric acid. One milliliter of this reagent is equivalent to 0.247 mg. of ethyl alcohol.

2. Sodium tungstate, 10% w/v.

3. Sulfuric acid, 2/3 *N*.

4. Tartaric acid, 10% w/v.

Procedure A for Blood, Urine, Saliva, Cerebrospinal Fluid, Tissue Distillates

1. Place specimen and reagents, as follows, into a 125-ml. distilling flask (a 250-ml. flask in the case of blood): 10 ml. of distilled water (20 ml. for blood analysis only); 2 ml. of the specimen (1-ml. specimens can be analyzed by collecting the distillate in a 5-ml. volumetric flask, proceeding with steps 3 through 5 as usual); 5 ml. of 2/3 *N* sulfuric acid; and 5 ml. of 10% sodium tungstate. Mix the contents by rotation and attach the flask to the distillation apparatus. Begin distillation when the blood has coagulated completely and has changed to a dark brown color.

2. Distill slightly less than 10 ml. directly into a 10-ml. glass-stoppered volumetric flask in about 8 to 10 minutes, using a microburner with a shielded 2.5-to-4-cm. flame. Make the distillate to the 10 ml. mark with distilled water, stopper, and mix thoroughly.

3. Into a 16-by-125-ml. borosilicate glass culture tube with Teflon-lined screw cap, place, in order, 1 ml. of distillate and 5 ml. of oxidizing reagent and mix by vigorous rotation. Immediately close the tube with the screw cap and heat for eight minutes in the 100 C fluid bath, immersing the tube above the liquid level.

TABLE 5.—*Weak Permanent Standards*

Nominal % Alcohol	Alcohol by Weight	Water, Ml.
0.000	0.00 ml.	2.00
0.005	1.00 ml. of 0.01% by weight	1.00
0.010	2.00 ml. of 0.01% by weight	0.00
0.013	0.52 ml. of 0.05% by weight	1.48
0.016	0.64 ml. of 0.05% by weight	1.36
0.019	0.76 ml. of 0.05% by weight	1.24
0.022	0.88 ml. of 0.05% by weight	1.12
0.025	1.00 ml. of 0.05% by weight	1.00
0.028	1.12 ml. of 0.05% by weight	0.88
0.031	1.24 ml. of 0.05% by weight	0.76
0.034	1.36 ml. of 0.05% by weight	0.64
0.037	1.48 ml. of 0.05% by weight	0.52

4. Cool the tube to room temperature (25 C or less) under running tap water or in an ice bath; mix the contents by rotation, and transfer a portion of the solution into a cuvette. Determine the photometric reading (optical density or per cent of transmittancy) at 450 mμ wave length, after setting the instrument at 100% transmittancy with a reference cuvette containing distilled water.

5. Obtain the alcohol concentration of the unknown specimen, in per cent weight/volume, from a calibration table or curve prepared by subjecting a series of biological specimens of known alcohol content to the entire analysis.

Procedure B for Tissues

1. Rapidly liquefy about 10 Gm. of frozen, or ice-cold, tissue in an ice-cold Waring blendor. Weigh out rapidly 2 Gm. of the liquefied sample to the nearest 0.01 Gm. and transfer quantitatively to a

250-ml. distilling flask with 30 ml. of 10% tartaric acid solution. Add 2 to 3 drops of antifoam fluid or use silicone antifoam compound (Dow Corning antifoam AF emulsion 30%, used as a 10% emulsion; Dow Corning antifoam A spray: Dow Corning Corp., Midland, Mich.; antifoam 60 emulsion, General Electric Co., Silicone Products Department, Waterford, N. Y.) or 0.1 Gm. of low-melting paraffin compound. Mix by rotation and attach flask to the steam distillation apparatus.

2. Distill in a rapid current of steam from a generator containing distilled water. Collect about 20 to 30 ml. of distillate in a 125-ml. distilling flask within 8 to 10 minutes.

3. To the 125-ml. distilling flask containing the above steam distillate add, in order, 5 ml. of ⅔ *N* sulfuric acid and 5 ml. of 10% sodium tungstate. Mix by rotation, attach to the distillation apparatus, and proceed as for biological liquids (steps 2-4 of procedure A).

4. Obtain the alcohol concentration of the tissue, expressed in percentage by weight, as in step 5, procedure A, from the same calibration table.

Special Procedures, C

1. Partially decomposed specimens are first distilled from the acid tungstate solution into another 125-ml. distilling flask, to which are then added 10 ml. of saturated aqueous mercuric chloride and 10 ml. of 10% calcium hydroxide suspension. This mixture is then redistilled and the analysis is completed as in procedure A.

2. Submicro and ultramicro determinations are carried out on fresh blood and urine specimens in Conway-type porcelain diffusion cells (catalog numbers 4472-F and 4472-H, Arthur H. Thomas Co., Philadelphia 5, Pa.). For submicroanalysis, 0.10 ml. of whole blood or urine is placed in the outer ring chamber of a 68-mm. diameter Conway unit, together with 1.00 ml. of saturated potassium carbonate to facilitate release of alcohol; 2.50 ml. of potassium dichromate oxidizing reagent is placed in the center well.

For ultramicroanalysis, 0.020 ml. of sample is placed in the outer ring chamber of a 44-mm. diameter Conway unit, together with 0.50 ml. of saturated potassium carbonate; 0.50 ml. of the above potassium dichromate oxidizing reagent is placed in the center well. The cell covers, lubricated with silicone stopcock grease, are applied, and the units are allowed to stand at room temperature of 12 hours, or at 38 C for 2 hours. The contents of the center well are then quantitatively transferred to microvolumetric flasks and made up with distilled water to 5 ml. or 2 ml. in the respective submicro or ultramicro methods. Photometry is carried out in the Beckman model DU spectrophotometer at 450 mμ, using silica microcuvettes whose light path is 10 mm. The alcohol concentration of the original specimen is obtained directly from calibration tables prepared by carrying a series of blood samples of known alcoholic content through complete analyses by the respective methods.

Critique.—The procedure resembles the Heise method; however, the distillation is improved; the test range, sensitivity, and specificity are extended; and the determination of color change after oxidation is made by spectrophotometry. The recovery of alcohol is from 99 to 100%, averaging 99.7%. The mean deviation between analyses on identical samples by different analysts in separate laboratories is 2.7% of the alcohol actually present (a mean absolute difference of ± 0.004% w/v ethyl alcohol). Alcohol-free blood and urine specimens consistently yield "blank" values less than 0.001% w/v alcohol; and acetone, chloral hydrate, chloroform, ethyl ether, lactic acid, and methenamine do not interfere in this analysis, although methanol and high concentrations of formaldehyde and of paraldehyde do react. The range of the method for a single analysis on unknown specimens is 0 to 0.61% w/v ethyl alcohol; however, higher alcohol concentrations in the original sample do not require a complete repeat analysis, since they can be determined by appropriate dilution of the remaining initial distillate. A single determination requires about 20 minutes. Up to five analyses per hour can be performed in series using a single distillation apparatus, and a single analyst can perform 8 to 12 determinations per hour by using two distillation units.

Harger Method

The Harger method [28] is as follows:

Principle.—Protein-free filtrates of blood, spinal fluid and tissues, and diluted urine are distilled from an all-glass still of small capacity. Alcohol in the distillate is oxidized to acetic acid by an accurately measured quantity of potassium dichromate in sulfuric acid at about 17 *N* acidity. The excess dichromate is accurately titrated with a standard solution of ferrous sulfate in the presence of methyl orange. The difference between this titration and that of a "blank" distillate containing no alcohol represents the quantity of dichromate used in the oxidation.

Apparatus

1. Distilling apparatus: 250-ml. round-bottom Pyrex flask and condenser of small capacity with straight glass condensing tube. The flask and condenser are connected, preferably, with standard taper ground-glass connections.

2. Volumetric flasks and pipettes: 5-ml. microburet graduated in 0.01 ml.

3. Beads or fragments of glass or Vitreosil to prevent bumping.

4. Reaction tubes: Pyrex test tubes, 25 by 200 mm., or 50-ml. Erlenmeyer flasks.

Reagents

1. Sodium tungstate, 10% w/v.

2. Sulfuric acid, 1/12 *N*.

3. Sulfuric acid, approximately 17 *N*: Pour, slowly with stirring, one volume of concentrated sulfuric acid into one volume of water; cool.

4. Sulfuric acid, concentrated.

5. Methyl orange, 0.1%: Dissolve 1 Gm. of methyl orange in 1 liter of approximately 0.025 *N* NaOH solution.

6. Ferrous sulfate solution: Place 50 Gm. of $FeSO_4 \cdot 7H_2O$, weighed to 0.1 Gm., in a 250-ml. volumetric flask containing 150 ml. of water. Carefully add 30 ml. of concentrated sulfuric acid; cool and dilute to the mark with water. Stopper and protect from light.

7. Ferrous sulfate–methyl orange standard solution: Into a 125-ml. Erlenmeyer flask, place 70 ml. of 17 *N* sulfuric acid, 30 ml. of 0.1% methyl orange solution, and exactly 2 ml. of ferrous sulfate solution. Two and one-half milliliters of this solution is equivalent to about 1 ml. of 0.0434 *N* dichromate. Standardize the solution each day. Keep the solution cool and prepare fresh solution after three or four days.

8. Standard potassium dichromate, 0.0434 *N*: Transfer 2.129 Gm. of C. P. potassium dichromate to a 1-liter volumetric flask. Dissolve in water and dilute to 1 liter. One milliliter of this solution is equivalent to 0.5 mg. of ethyl alcohol.

Procedure

1. Prepare the usual 1:10 protein-free tungstic acid filtrate, using 2 ml. or more of blood or spinal fluid, or 2 Gm. or more of minced tissue. For example, to 5 ml. of blood add 40 ml. of 1/12 *N* sulfuric acid, followed by 5 ml. of 10% sodium tungstate solution. Mix. Let stand a sufficient time, with occasional mixing, to allow complete diffusion of alcohol throughout the flask. Filter. Dilute urine tenfold with water. The alcohol in tissues is preferably removed by steam distillation.

2. Pipet 10 ml. of blood filtrate or diluted urine (representing 1 ml. of sample) into a 250-ml. flask. Add 40 ml. of water and a few glass beads or fragments. Connect the flask with the condenser and carefully heat the contents with a microburner flame. Collect almost 50 ml. of distillate through a condenser outlet which dips nearly to the middle of a 50 ml. glass-stoppered cylinder or volumetric flask. Dilute to the 50 ml. mark. Mix.

3. Pipet 10 ml. of the diluted distillate (representing 0.2 ml. or 0.2 Gm. of sample) into a 50-ml. Erlenmeyer flask or 25-by-200-mm. test tube. Add exactly 2 ml. of 0.0434 *N* dichromate solution and then 10 ml. of concentrated sulfuric acid. Mix well; cover with small beaker and allow to stand exactly 10 minutes. Cool in a bath of cold running water.

4. Simultaneously prepare several reagent blanks by substituting 10 ml. of distilled water for 10 ml. of distillate in step 3, using 1 ml. (titration B_1) and 2 ml. (titration B_2) of 0.0434 *N* dichromate.

5. Titrate the excess of dichromate with the ferrous sulfate–methyl orange reagent (in a microburet). The yellow color fades as the chromate ion is reduced. Then, when the first excess drop of reducing solution is added, the pink color of methyl orange fills the solution and makes a sharp endpoint.

6. If the sample titration in step 5 is less than 0.2 ml., repeat the distillation using 5 ml. of protein-free filtrate or oxidize less than 5 ml. of original distillate by substituting distilled water for an appropriate portion of the distillate.

7. Standardize the procedure against specimens and aqueous solutions of known alcohol content.

Calculations.—Let B_1 and B_2=the blank titrations of 1 and 2 ml., respectively, of 0.0434 *N* dichromate (step 4), and let U=the sample titration (step 3). Further, let S=milliliters or grams of sample represented by the sample titration. Then, B_2-B_1=milliliters of ferrous sulfate solution equivalent to 1 ml. of the 0.0434 *N* dichromate. The difference between blank titrations is determined in order to correct for impurities in the water and reagents and for the extra drop to obtain the endpoint. Hence $(B_2-U) \div (B_2-B_1)$=milliliter of 0.0434 dichromate required for the oxidation of alcohol. Since 1 ml. of the dichromate is equivalent to 0.5 mg. of ethanol,

$$\% \text{ alcohol in original sample} = \frac{0.5\ (B_2-U)}{10S\ (B_2-B_1)}.$$

Critique.—This is perhaps the most widely used laboratory method. It requires simple and inexpensive apparatus. The distillation equipment permits rapid boiling and efficient recovery. The salient feature of the method is the final titration which has a sharp and distinctive end-point. The titration procedure is used in several other methods described in the literature. The range of concentrations of alcohol is up to 0.50% w/v; the speed of determinations and the recovery, specificity, and precision are within the same limits as those of the Dubowski procedure A described above.

Friedemann and Brook Method

The Friedemann and Brook method[10] is as follows:

Principle.—Blood, urine, or tissues are distilled directly or with steam from an acid–sodium tungstate–mercuric sulfate medium (removing volatile amines and some aldehydes, paraldehyde, and ketones). The distillate is redistilled from calcium hydroxide and mercuric sulfate (removing most phenols and the remaining aldehydes and ketones). The alcohols in the distillate are oxidized to the respective acids (formic, acetic, etc.) with potassium dichromate and sulfuric acid at about 2 *N* acidity. The volatile acids are quantitatively distilled from saturated magnesium sulfate solution. A portion of the distillate is titrated directly with standard sodium hydroxide; another portion is titrated after extraction with a measured volume of organic solvent, from which the distribution coefficient may be calculated. The two titrations identify

and determine ethyl alcohol and higher alcohols. Methyl alcohol is determined quantitatively by titration of formic acid.

Apparatus

1. Distillation apparatus: All-glass, for direct and steam distillation similar to that used in the Dubowski and Harger methods. (Obtainable from Aloe Scientific Division, A. S. Aloe Co., 5655 Kingsbury Ave., St. Louis 12, Mo.)

2. Soda lime tower: Glass tube, 3 by 48 in., filled with soda lime between cotton plugs, used for aeration of distillates with carbon dioxide–free air.

3. Separatory funnel: Squibb separatory funnel, Pyrex glass, 250 ml. glass-stoppered.

4. Volumetric ware: Good grade of pipets, burets, and glass-stoppered volumetric flasks.

Reagents

1. Calcium hydroxide suspension: Slake 100 Gm. of pure calcium oxide with a minimum of water; add 1 liter of water. Keep the creamy suspension in a glass-stoppered bottle protected from dust.

2. Distilled water, free of volatile impurities.

3. Ethyl ether, anhydrous.

4. Magnesium sulfate.

5. Mercuric oxide, red powder.

6. Mercuric sulfate reagent, 10% w/v in 2 *N* sulfuric acid.

7. Potassium dichromate, powdered.

8. Sodium hydroxide, 0.10 *N* stock solution, protected from atmospheric carbon dioxide.

9. Sodium hydroxide, 0.010 *N*, freshly prepared from the 0.10 *N* stock solution with boiled, distilled water.

10. Sodium tungstate solution 10% w/v.

11. Sulfuric acid, 20 *N*.

12. Sulfuric acid, 10 *N*.

Procedure

1. Into a 500-ml. distillation flask containing 100 ml. of distilled water and 15 ml. of acid mercuric sulfate reagent, place 1 to 10 ml. of blood or urine (or 1 to 10 Gm. of finely ground tissue), 10 ml. of sodium tungstate solution, and some talcum. Mix contents thoroughly by rotation.

2. Distill rapidly until the volume has been reduced about one-half or more, collecting the distillate 1 in another 500-ml. distillation flask.

3. Add to this distillate 1, 10 ml. of acid mercuric sulfate reagent, 10 ml. of calcium hydroxide suspension, talcum, and enough distilled water to bring the volume to about 100 ml. If the sample contains paraldehyde, phenol, or other volatile substances than alcohols, the contents of the first and second distillation flasks should be well shaken and allowed to stand for at least 10 minutes before each distillation.

4. Distill the mixture, receiving 70 to 80 ml. of distillate 2 in a glass-stoppered 100-ml. volumetric flask. Add 10 ml. of 20 *N* sulfuric acid and an excess of powdered or dissolved potassium dichromate. Allow the well-mixed reaction mixture (which contains about 2 *N* acid) to stand overnight at room temperature, or heat for about 30 minutes in a boiling water bath and then cool.

5. Transfer the oxidation mixture to a 500-ml. distillation flask; add distilled water to bring the mixture volume to about 200 ml. Then add about 50 gm. of magnesium sulfate crystals and talcum. The magnesium sulfate reduces the acidity, prevents overoxidation when the volume becomes small, and greatly increases the volatility of the acetic and other acids. Distill the mixture and collect 180 to 190 ml. of distillate 3 in a 500-ml. distillation flask.

6. Aerate the distillate 3 with air from the soda lime tower to remove carbon dioxide and titrate the total volatile acids to the phenolphthalein endpoint with 0.01 *N* sodium hydroxide (titration A). (Aqueous sodium phenolphthaleinate is preferred to the alcoholic indicator solution.)

7. If the presence of methyl alcohol or other alcohols is suspected, treat the distillate 3, after titration A, with talcum, 2 ml. of 10 *N* sulfuric acid, 50 Gm. of magnesium sulfate, and 0.3 to 0.5 Gm. of mercuric oxide in that order; and redistill in 30 to 45 minutes, collecting the distillate 4 in a 250-ml. volumetric flask which is then made to the mark with distilled water. This quantitatively removes formic acid, which is produced in a constant 60% yield from methyl alcohol.

8. Titrate directly 100 ml. of distillate 4 with 0.01 *N* sodium hydroxide after aeration to remove carbon dioxide (titration B).

9. Extract another 100 ml. of distillate 4 with 50 ml. of ethyl ether in a 250-ml. Squibb separatory funnel, shaking for one minute or more. Draw off the aqueous phase and titrate it with 0.01 *N* sodium hydroxide (titration C).

10. The procedure may be considerably simplified, if it is known that only ethyl alcohol is present, by doing only two distillations and one titration, as follows, according to steps 1, 2, and 4 through 6: (*a*) distillation of alcohol from mercuric sulfate–tungstic acid, (*b*) distillation of volatile acids following oxidation, and (*c*) titration of total volatile acids by titration A.

11. In all sample titrations (A, B, and C) corrections for acids, if any, derived from reagents are made by titrations of blank distillates.

12. The procedure is standardized against aqueous solutions and blood containing known quantities of ethyl alcohol or other alcohols.

Calculation of Results.—The difference between titrations A and B determines the formic acid from oxidation of any methyl alcohol present. Titration B determines the volatile acids derived by oxidation from alcohols other than methyl alcohol. Titrations B and C determine the distribution constant $k=(C/B\times 100)$, which is characteristic for the acid derived from each alcohol and which represents the percentage of acid remaining in the aqueous

phase. Thus the constant for acetic acid from ethyl alcohol, or the percentage of acid not extracted= 86.5; for acids from propyl alcohol=70.0; for acids from butyl alcohol=49.0.

When titration A equals titration B, the sample contains no methyl alcohol. If, in addition, k is 86 to 87, the sample contains only ethyl alcohol.

Critique.—The distinctive feature of this method is the ability to identify and determine specifically ethyl alcohol and other alcohols which may be present in the sample. Most potential interferents are eliminated in the double distillation. With 2-ml. samples the minimum alcohol concentration at which the method is still reliable is about 0.050 ± 0.0015% ethyl alcohol or methyl alcohol and with 5-ml. samples about 0.020 ± 0.0006% (steps 1 through 6). The over-all recovery is within 99% in the four distillations of the complete procedure. The accurate range of the method is very wide, from 0.02 to about 1.0% of alcohol in the sample. The complete procedure is longer and more involved than the three previously described methods. A single determination requires about three hours. However, if the determination is limited to only two distillations and one titration (step 10), about 90 minutes are required for a determination.

QUALITATIVE TESTS FOR SOME COMMON INTERFERING SUBSTANCES

The identity and significant concentrations of possible chemical interferents vary with the particular method chosen for the determination of ethyl alcohol, depending on the relative specificity or selectivity of that method for ethyl alcohol. When present, such interference consists of the production of falsely positive apparent ethanol reactions, or of false elevations of a true ethanol level. The presence of significant concentrations of any potential chemical interferents, in body materials obtained from living subjects, is a comparatively infrequent occurrence, particularly when the subjects are conscious and well. It is even more unusual to find significant levels of two or more potential chemical interferents in a single biological material specimen from a living subject, in addition to ethyl alcohol. However, it is frequently necessary or desirable in forensic alcohol determinations to establish experimentally the absence of such potential interferents in significant concentrations in order to safeguard their probative value; and it is occasionally useful to search for the more common nonethanol volatile organic substances in clinical alcohol analyses conducted in connection with the differential diagnosis of coma states.

Among the volatile substances most commonly encountered in actual or suspected interference with some alcohol determination methods, when present in sufficient quantity, are acetaldehyde, acetone, formaldehyde, isopropyl alcohol, methyl alcohol, and paraldehyde. The following simple tests will generally suffice for indicating the presence or absence in body material specimens of concentrations of these six substances potentially capable of interference in some, though not all, ethyl alcohol determination methods. These screening tests are not intended to cover every substance potentially capable of chemical interference in some alcohol analysis, nor is inclusion of a test for a given substance an indication that it can or will interfere in any particular ethanol determination method.

Obviously, if these or other tests disclose the presence of significant levels of potentially interfering substances in a specimen to be analyzed for ethyl alcohol content, the possibility of such interference should be eliminated by choosing a method unaffected by the interferent(s) present or by adequately modifying the proposed alcohol procedure. Should this be impossible or impractical, or should the specimen appear unsuitable for alcohol analysis because of advanced decomposition, putrefaction, or especially great chemical contamination, it is generally preferable to forego that alcohol analysis rather than to jeopardize the validity of the results.

An important application of these screening tests is in clinical alcohol analysis practice under the following two conditions: (1) in the event of lack of concordance between a confirmed ethyl alcohol analysis result and the subject's physical condition, and (2) in comatose or seriously intoxicated subjects, to avoid a false sense of security based on, and a misleading clinical interpretation given to, a positive ethyl alcohol analysis result, in the presence of another unrecognized concurrent intoxication (e. g., by methyl alcohol).

Acetaldehyde Test

Acetaldehyde is detectable in biological materials and distillates by its distinctive pungent odor at concentrations below 0.01%, as is paraldehyde, which is hydrolyzed during distillation and appears in the distillate as acetaldehyde. The following chemical screening test identifies acetaldehyde in significant concentrations.

Reagents

1. Acetic acid, glacial, C. P.
2. Piperidine (hexahydropyridine).
3. Sodium nitroferricyanide, saturated solution, freshly prepared.

Procedure

1. To 1 ml. of unoxidized body material distillate in a small borosilicate glass test tube, add 1 drop of freshly prepared sodium nitroferricyanide solu-

tion to give a pale yellow color to the solution; then allow 1 drop of piperidine to flow down the side of the inclined tube. Shake the tube to mix the contents, and observe the resulting solution color.

2. Add 3 to 4 drops of glacial acetic acid; mix by shaking and observe for color changes.

Test Interpretation

Negative: A yellow to light brown color is obtained in step 1, which changes to a slightly lighter shade of yellow on addition of glacial acetic acid. (Formaldehyde does not react in this test.)

Positive: A green to deep blue color, depending on the concentration of acetaldehyde, is obtained within two minutes in step 1; it changes to deep green on addition of glacial acetic acid and then fades.

Sensitivity.—The test becomes positive at acetaldehyde concentrations of 0.005% or higher in the distillate.

Acetone Test

Acetone is readily detectable in body material distillates at concentrations considerably below those interfering in most alcohol determination methods, by use of commercial urine acetone test materials based on Rothera's test.

Reagent.—Acetest reagent tablets, containing aminoacetic acid, disodium phosphate, and sodium nitroferricyanide (catalog number 2381, Ames Co., Inc., Elkhart, Ind.).

Procedure

1. Place 1 Acetest reagent tablet on a clean piece of white paper. Place 1 drop of distillate on the tablet.

2. Observe the tablet for color changes after 30 seconds.

Test Interpretation

Negative: Tablet color remains unchanged or tablet becomes pale cream colored.

Positive: Tablet surface changes within 30 seconds to a color varying from light lavender to deep purple, depending on the acetone concentration present.

Sensitivity.—The test becomes positive at acetone concentrations below 0.01% in the distillate.

Formaldehyde Test

Formaldehyde is readily detectable in biological material distillates by a sharp recognizable odor even at low concentrations (below 0.02%) and is demonstrable by simple specific chemical tests at far lower levels.

Reagents

1. Chromotropic acid disodium salt: 4,5-dihydroxy-2,7-naphthalene-disulfonic acid disodium salt, Practical (catalog number P230, Distillation Products Industries Division, Eastman Kodak Co., Rochester 3, N. Y.).

2. Sulfuric acid, concentrated, C. P.

Procedure

1. To 1 ml. of biological material distillate in a small borosilicate glass test tube, add approximately 10 mg. of chromotropic acid disodium salt and mix thoroughly by shaking.

2. Add 1.5 ml. of concentrated sulfuric acid along the side of the inclined test tube so as to underlay the aqueous solution. Examine the interface for a purple or violet color.

3. Cautiously mix the tube contents by gentle swirling, and allow the tube to stand for approximately five minutes. Examine for presence of a diffuse purple or violet color.

Test Interpretation

Negative: Colorless or yellow color at the interface (step 2) and a colorless or yellow mixture (step 3). (Acetaldehyde does not react in this test.)

Positive: Presence of a purple or violet color at the interface (step 2) and a purple or violet color in the mixture (step 3).

Sensitivity.—The test becomes positive at formaldehyde concentrations below 0.00005% in the distillate.

Isopropyl Alcohol Test

Isopropyl alcohol can be identified in acetone-free body material distillates by a simple modification of Denigès' procedure,[ab] sensitive to concentrations below interfering levels.

Reagent.—Denigès' reagent: Suspend 2 Gm. of yellow mercuric oxide in 16 ml. of distilled water and, while mixing, add 8 ml. of concentrated sulfuric acid. Stir and dissolve with addition of another 16 ml. of distilled water.

Procedure

1. To 1 ml. of distillate in a small borosilicate glass test tube add 2 ml. of Denigès' reagent. Stopper the test tube and heat in a fluid bath at 100 C for 30 minutes.

2. Cool the tube and examine for presence of a white finely divided precipitate, centrifuging the tube if necessary.

Test Interpretation

Negative: No white precipitate or white turbidity is present.

Positive: A distinct white precipitate is present. (Acetone also yields a positive test and is ruled out by the acetone test described above.)

Sensitivity.—The test becomes positive at isopropanol concentrations of 0.005% in the distillate.

Methyl Alcohol Test

Methyl alcohol, which interferes in most ethyl alcohol determination methods, can be identified readily and, in the absence of formaldehyde, specifically at extremely low concentrations in biological material distillates by a simple modification of Eegriwe's chromotropic acid test for formaldehyde.

Reagents

1. Acid permanganate reagent: 3.0% potassium permanganate in 12.8% phosphoric acid (15 ml. of 85% syrupy phosphoric acid per 100 ml.).

2. Chromotropic acid disodium salt: 4,5-dihydroxy-2,7-naphthalene-disulfonic acid disodium salt, Practical.

3. Sodium bisulfite ($NaHSO_3$), C. P., powdered.

4. Sulfuric acid, concentrated, C. P.

Procedure

1. Into a small borosilicate glass test tube place 1 ml. of biological material distillate; add 0.1 ml. (approximately 2 drops) of acid permanganate reagent, shake well to mix, and allow to stand at room temperature for two minutes.

2. Add just enough powdered sodium bisulfite to decolorize completely the excess potassium permanganate and any brown manganese dioxide formed (approximately 5 to 10 mg.).

3. Add approximately 10 mg. of chromotropic acid disodium salt and shake gently to dissolve; then add 1.5 ml. of concentrated sulfuric acid, allowing the acid to flow down the side of the inclined test tube to form a separate layer below the aqueous solution. Examine the interface for presence of a purple or violet color.

4. Cautiously mix the tube contents by gentle swirling and allow the tube to stand for approximately five minutes. Examine for presence of a diffuse purple or violet color.

5. In all positive methyl alcohol tests, also test the unoxidized distillate for formaldehyde as described above.

Test Interpretation

Negative: Absence of a purple or violet color at the interface (step 3) or of a diffuse purple or violet color (step 4) indicates the absence of methyl alcohol and of formaldehyde. (The solution may be colorless or yellow to light brown.)

Positive: Presence of a purple or violet color at the interface (step 3) or of a diffuse purple or violet color (step 4) indicates the presence of methyl alcohol or of formaldehyde in the distillate, the color intensity being proportional to the concentration. (The presence of formaldehyde in the distillate can be ruled out by the formaldehyde test described above; i. e., by a negative result following steps 3 and 4 of this test performed on 1 ml. of unoxidized distillate.)

Sensitivity.—The test as described becomes positive at methanol concentrations of less than 0.0002% in the distillate.

Appendix B

PROCEDURES FOR ANALYSIS OF BREATH FOR ETHYL ALCOHOL

Alcometer

The Alcometer (originally called Alcoholometer) (fig. 1), developed by Greenberg and Keator,[8] is a fully automatic apparatus (manufacturer: Frederick G. Keyes, Inc., 243 Broadway, Cambridge, Mass.), based on use of the iodine pentoxide reaction of Haggard and Greenberg,[3] in which the cycle of events is controlled by a synchronous electric motor.

The major components of the analytical train are as follows (fig. 2): (1) a pump supplying room air to purge the instrument and to sweep the sample through the analytical system; (2) a silica gel drying tube no. 1 for drying incoming room air; (3) an iodine pentoxide reaction tube no. 1 to oxidize any interfering substances in the incoming room air; (4) a bulb, containing powdered copper, to absorb any liberated iodine; (5) a drying tube no. 2 to insure complete dryness of the purified room air; (6) a fixed volume sample chamber, with solenoid valves; (7) an iodine pentoxide tube no. 2 to oxidize any alcohol present in the breath sample; (8) a glass or plastic bubbler tube leading from the second reaction tube into the indicator solution; (9) an indicator solution vial containing starch–potassium iodine to react with any iodine released in the iodine pentoxide oxidation in tube no. 2; and (10) a photronic colorimeter consisting of two barrier layer photocells, a photometer lamp, and a microammeter calibrated directly in blood alcohol concentration.

In addition to the Alcometer, the following expendable materials are required for each test: one indicator vial containing 0.1% starch and potassium iodine solution in a vial which also serves as a photometer cuvette and one wood mouthpiece.

The analysis consists of four principal phases: (1) purging of the sample chamber and chemical train with purified room air; (2) collection of a measured volume of alveolar air; (3) pumping of the breath sample through the hot iodine pentoxide reagent bed and flushing of any liberated proportionate quantity of iodine vapor into the 0.1% starch indicator solution; and (4) measurement of the resulting blue color of the indicator solution with an integral photoelectric colorimeter, on which a reading, proportionate to the alcohol concentration of the breath sample, is obtained on a microammeter scale, calibrated directly in blood alcohol concentration.

Alcohol is oxidized as follows by the iodine pentoxide:

$$(a)\quad 5C_2H_5OH + 6I_2O_5 = 10CO_2 + 15H_2O + 6I_2$$

$$(b)\quad C_2H_5OH + I_2O_5 = 2CO_2 + H_2O + 2HI$$

At a constant temperature and a constant rate of air flow, the yield of iodine is consistently proportional to the quantity of ethyl alcohol oxidized.

Various mechanical and electrical components operate the instrument through the proper sequence of steps according to predetermined timing; interlocks prevent untimely operation or omission or

duplication of steps in the analysis. The initial warm-up of the instrument requires about 10 minutes, and a complete analysis thereafter requires about 8 minutes.

Alcotest

This portable device (fig. 3), developed by Grosskopf and Scheibe,[21] utilizes the vapor-in-air detector tube system of Grosskopf and employs potas-

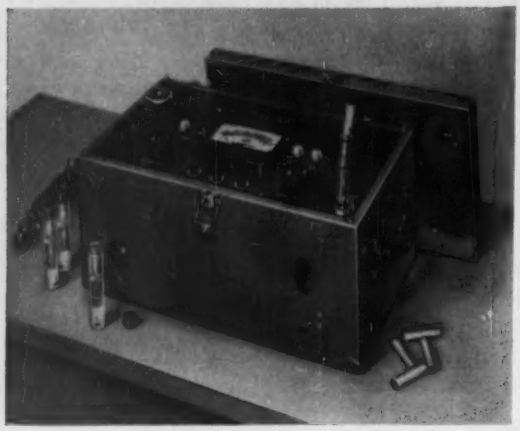

Fig. 1.—The Alcometer, model M-4.

sium dichromate in sulfuric acid for oxidation of alcohol in mixed expired breath (manufacturer: Drägerwerk, Lübeck, Germany; U. S. distributor: Schueler and Company, 75 Cliff St., New York 38, N. Y.).

A single test unit consists of an expendable sealed glass detector tube, an expendable plastic mouthpiece, and a sturdy plastic breath-measuring bag of 1 liter capacity. The detector tube is a 9.5-mm. diameter glass tube, 85 mm. long, containing a 15-mm. long reagent layer of silica gel impregnated with potassium dichromate in sulfuric acid solution held between glass wool plugs. A 1-mm. wide annular marking of yellow color approximating that of the reagent zone before the test encircles the tube in the middle of the reaction layer.

Alcohol is oxidized as follows:

$$2K_2Cr_2O_7\,(\text{yellow}) + 8H_2SO_4 + 3C_2H_5OH = 2Cr_2(SO_4)_3\,(\text{green}) + 2K_2SO_4 + 3CH_3COOH + 11H_2O$$

The reaction is accompanied by a color change from the yellow of the potassium dichromate to the green of the chromic sulfate, the width of the green zone being roughly proportional to the breath alcohol concentration. The approximate lower sensitivity of the original test is at about 0.08 mg. of alcohol per liter of tested air (corresponding in this test system to about 0.03% w/v blood alcohol), and the maximum recognizable upper test range is at about 0.5 mg. of alcohol per liter (corresponding to about 0.17% w/v blood alcohol). In accordance with the suggestions of one of us (K. M. D.), a special Alcotest 1.5 unit was later developed for United States practice.

The flow resistance of the tube (1 liter per minute at 35 to 55 mm. H_2O pressure) is such that in actual use 1 liter of expired breath is generally forced through in about 15 seconds, requiring the test subject's full lung pressure and preventing aspiration and admixture of room air. The absorbed water vapor from the breath reacts with the concentrated sulfuric acid in the reagent layer to produce a temperature of about 80 C, which increases the speed of the reaction and heats the glass reaction tube sufficiently to prevent condensation of breath prior to its passage through the reagent zone.

The test operation consists of three steps: 1. Both ends of the detector tube are cut off. A plastic mouthpiece is placed on one end, and the other end is inserted (in the direction indicated by an arrow on the tube) into the plastic air inlet of the completely deflated plastic bag for collecting and measuring 1 liter of air. 2. The 1-liter test bag is inflated by the subject with mixed expired breath through the mouthpiece and detector tube, if possible with a single breath, in not more than 20

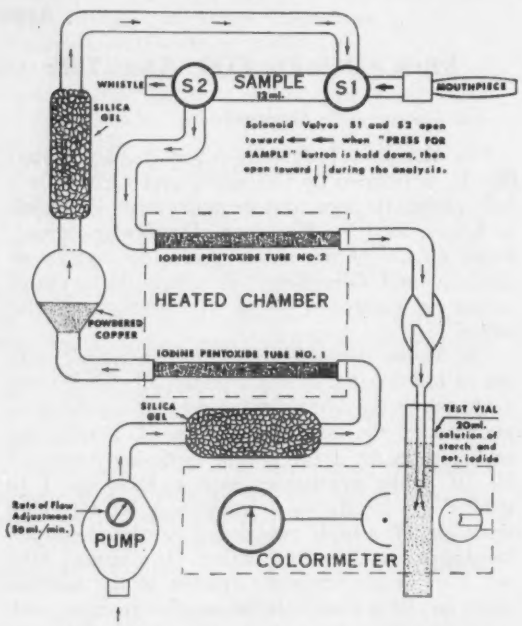

Fig. 2.—Schematic diagram of the Alcometer.

seconds. 3. The reaction zone of the detector tube is examined to determine whether any discoloration of the originally yellow reagent layer to green has occurred, and if so its extent.

Rough semiquantitative interpretation of any color change noted in the Alcotest 1.5 detector tube can be made as follows: At no discernible green

discoloration the probable blood alcohol level of the test subject is less than 0.05% w/v. A green coloration of the reaction zone up to the yellow marking ring (about 8 mm.) indicates a probable blood alcohol level of 0.05 to 0.15% w/v. A green coloration of the reaction zone beyond the yellow comparison ring indicates that the probable blood alcohol level of the test subject is above 0.15% w/v.

A complete test requires about one minute. The test materials are packaged in a small cardboard carton containing 10 detector tubes, 10 cellophane-wrapped sterilized plastic mouthpieces, an ampul-tip breaker, and one plastic breath-measuring bag, together with a direction booklet and a color comparison chart. The shelf life of the unit is stated to be at least two years.

The Alcotest is designed only for use as a preliminary breath alcohol screening test.

Breathalyzer

The Breathalyzer (fig. 4) (distributor: Stephenson Corporation, Red Bank, N. J.) was developed by Borkenstein [23] and utilizes potassium dichromate in sulfuric acid solution as the reagent for oxidizing alcohol in alveolar air. The operation consists of four principal phases (fig. 5): (1) flushing of the apparatus with room air; (2) collecting a measured volume of alveolar air; (3) passing the breath sample through potassium dichromate–sulfuric acid solution in an ampul-cuvette and allowing oxidation to proceed; and (4) measuring the resulting color change of the reagent with an integral photoelectric filter photometer. The increased light transmission through the test ampul, resulting from the color change from the yellow of the dichromate to the green of the chromic sulfate, is measured with a balanced electrical circuit from two photovoltaic cells, using the Bunsen principle. A light bulb is mounted on a movable carriage between the ampuls, and the distance the light must be moved to reestablish the original photometric balance between light transmission through the ampuls prior to analysis is registered by the movement of a coupled pointer across a scale calibrated directly in blood alcohol concentration.

Fig. 3.—The Alcotest unit.

Fig. 4.—The Breathalyzer.

In addition to the Breathalyzer apparatus in its self-contained aluminum carrying case, the following expendable materials are required for each test: (1) two Breathalyzer reagent ampuls containing 3.0 ml. of 0.025% potassium dichromate in 50 vol.% sulfuric acid (one ampul serves as a photometric standard and is reusable; the ampuls also serve as photometer cuvettes), (2) one glass capillary bubbler tube for delivering the breath sample into the reagent ampul, and (3) a plastic mouthpiece and saliva trap.

A complete analysis requires about 6 minutes, and the initial warm-up of the instrument requires about 20 minutes. The Breathalyzer is designed for quantitative breath alcohol determination.

Drunkometer

The Drunkometer (fig. 6) (distributor: Stephenson Corporation, Red Bank, N. J.), developed by Harger and associates,[8] is a portable apparatus which also incorporates provisions for performing a rapid semiquantitative breath alcohol screening test. Potassium permanganate in sulfuric acid solution is used to quantitate the alcohol from samples of mixed expired breath or rebreathed air.

The apparatus consists of the following main components (fig. 7): (1) a rubber balloon for collection of the breath sample; (2) the alcohol reaction unit, consisting of an ampul containing sulfuric

acid and potassium permanganate, connected to the balloon through a glass capillary tube and mounted in front of an electrically illuminated window between two color comparison standards

Pa.) and a carbon dioxide–absorbing tube of Ascarite (a sodium hydroxide asbestos absorbent, supplied by Arthur H. Thomas Co., Philadelphia 5, Pa.).

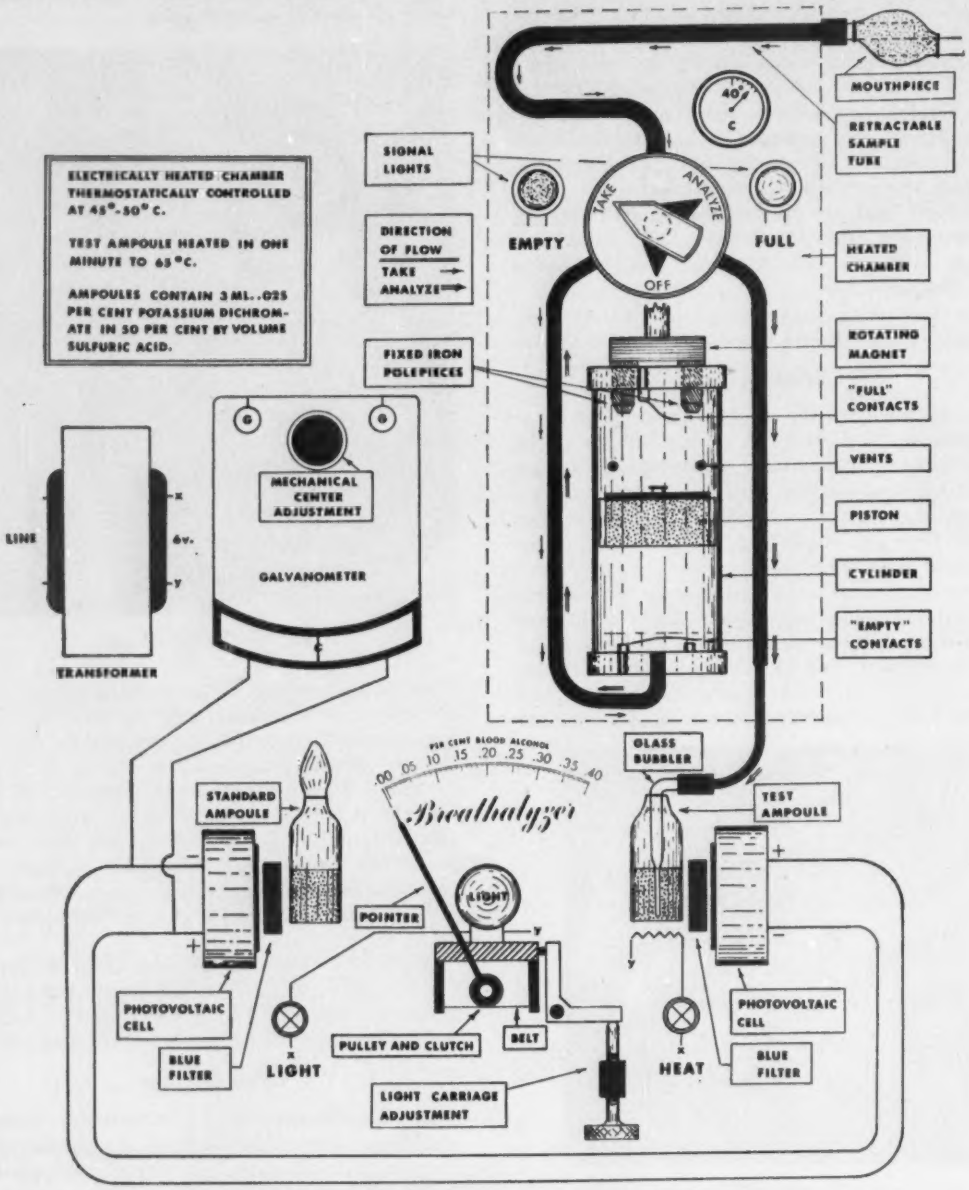

Fig. 5.—Schematic diagram of the Breathalyzer.

in similar ampuls; (3) a breath-quantity measuring system consisting of a two-way valve, a water displacement gasometer, and an alternate chemical train of a moisture-absorbing tube of Dehydrite (an anhydrous granular magnesium perchlorate, supplied by Arthur H. Thomas Co., Philadelphia 5,

In addition to the self-contained apparatus, the following expendable materials are required for each test: (1) a rubber balloon with wood mouthpiece; (2) a sealed glass ampul reaction tube containing 10 ml. of 16 *N* sulfuric acid, to which 1.0 ml. of *N*/20 potassium permanganate solution is

added immediately prior to an analysis; and (3) a 4-mm. glass inlet bubbler tube with rubber sleeve for making gas-tight connections between the ampul, the breath inlet tube, and the gasometer.

The Drunkometer can be used as a preliminary rapid semiquantitative screening test employing mixed expired breath or for quantitative determinations employing mixed expired breath or rebreathed air. In each instance, a fixed quantity of ethyl alcohol (0.169 mg.) is measured and the volume of mixed expired breath or rebreathed air required to furnish this quantity of alcohol is determined by direct water displacement, or the volume of alveolar air is calculated from the weight of carbon dioxide absorbed.

The analysis consists of the following major phases: (1) collection of a suitable breath sample by inflation of a rubber balloon with mixed expired breath or rebreathed air; (2) passage of the sample through the alcohol reagent in the ampul reaction tube until the original purple permanganate color has reached a pink-yellow end-point intermediate between the pink and yellow color standards, or until about 2,000 ml. of breath have passed through the apparatus (indicating a probable blood alcohol level of not more than 0.03%); (3) measurement of the breath volume required to reach the end-point (and which, therefore, contained 0.169 mg. of ethanol) by one of the following procedures: 1. Semiquantitative ("volumetric") test using mixed expired breath and quantitative determination using rebreathed air: The breath after leaving the reaction ampul passes directly to the graduated gasometer, where it displaces an equal volume of water. The breath volume used is read directly from the gasometer. 2. Quantitative determination using mixed expired breath: The breath after leaving the reaction ampul passes through the Dehydrite and through the previously weighed Ascarite tube, which absorbs the carbon dioxide present and is later reweighed to determine the carbon dioxide quantity absorbed during the test.

Calculations.—Since in all three variations of the tests (table 3), the quantity of alcohol required to reach the end-point (0.169 mg.) is identical, only the breath volume used for each test needs to be determined to supply the basic information concerning breath alcohol concentration. This is, in turn, converted to blood alcohol concentration using the observations that the weight of alcohol present in 1 ml. of blood is equal (*a*) to that present in about 3,200 ml. of mixed expired breath after removal of carbon dioxide and collection over water at 25 C or (*b*) to that present in 2,100 ml. of alveolar breath or in 2,100 ml. of rebreathed air or (*c*) to that accompanying 190 mg. of carbon dioxide from mixed expired breath or from alveolar breath. A complete "volumetric" Drunkometer test requires about 5 to 8 minutes; the complete quantitative determination requires about 10 minutes, including time for weighing the Ascarite tube before and after the test.

Drunkotester

The portable Drunkotester (manufacturer: Komyo Chemical Industrial Co., Ltd., Meguro, Tokyo, Japan; distributor: Kongo Shoji Kaisha, Ltd., Central P. O. Box No. 1253, Tokyo, Japan), developed by Kobayashi and Kitagawa, utilizes potassium dichromate in sulfuric acid solution to oxidize the alcohol in mixed expired breath.

The equipment consists of an expendable rubber balloon, an expendable sealed glass alcohol detector tube, a metal piston pump with two-way valve measuring 50 ml. per piston stroke, and a compari-

Fig. 6.—The Drunkometer.

son chart—all contained in a small metal carrying case. The detector tube is a 4-mm.-diameter glass capillary tube, 12 cm. long, containing five narrow reagent zones of silica gel impregnated with potassium dichromate in sulfuric acid solution which are separated by 1 cm. long layers of powdered glass.

In the operation, the ends of the glass detector tube are cut off and a rubber balloon is inflated by the subject with mixed expired breath. One end of the detector tube is inserted into the rubber balloon outlet, the other into the pump inlet opening. The pump valve is opened and 50 ml. of breath are aspirated from the ballon through the detector tube in approximately 15 seconds. The pump valve is then reversed; the piston is returned to the initial position; the valve is reopened, and another 50-ml. breath sample is aspirated through the detector

tube. The tube is then disconnected and warmed briefly over an open flame (burner, match, cigarette lighter, etc.). The number of reagent zones which have changed from their original yellow color are noted by comparison with an unused tube, and the color intensity of the several changed zones (various shades of orange, green-yellow, and blue-green) is compared with a color chart depicting 12 tubes in various stages of change corresponding to blood

ter,[36] is a portable device for quantitatively absorbing both alcohol and carbon dioxide from exhaled breath which may be obtained in the field and later analyzed in the laboratory, combined with an integral system for performing a preliminary on-the-spot breath alcohol screening test.

The breath collection system is based on the organic vapor-absorbing properties of magnesium perchlorate. In principle, the method depends on

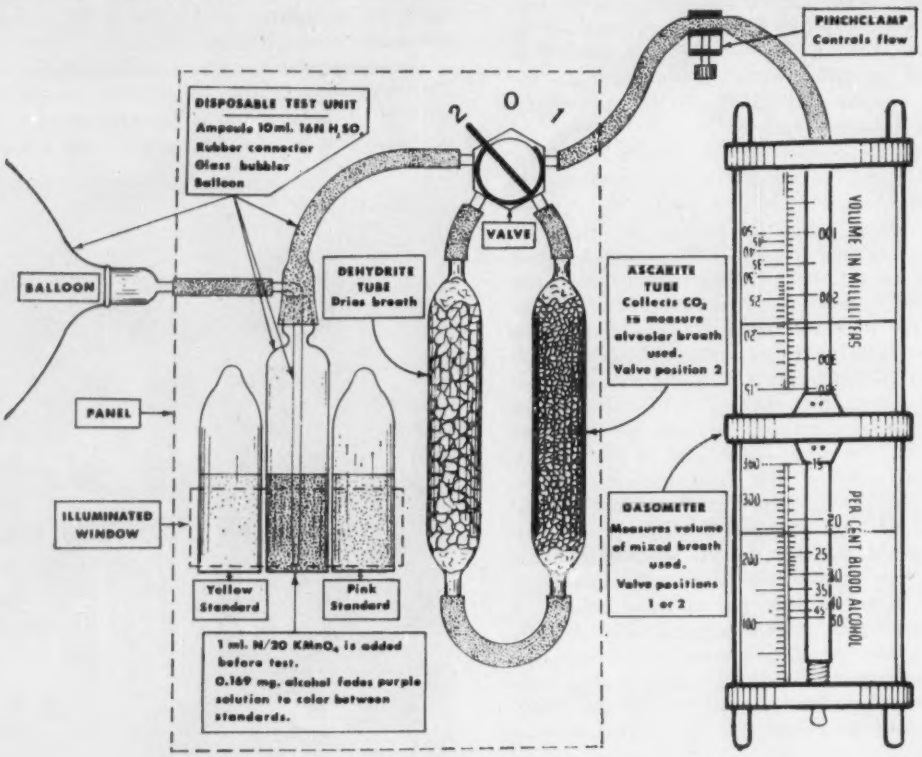

Fig. 7.—Schematic diagram of the Drunkometer.

alcohol levels of 0.00 to 0.42% in steps of 0.03 or 0.04%. A complete test requires about three to five minutes.

The system is restricted to use as a preliminary breath alcohol screening test.

Intoximeter

The Intoximeter (fig. 8) (manufacturer: Intoximeter Association, 334 Buffalo Ave., Niagara Falls, N. Y.), developed by Jetter, Moore, and Forres-

the complete absorption of alcohol and of water vapor from a mixed expired breath sample by magnesium perchlorate, followed by the quantitative absorption of carbon dioxide by Ascarite.

Each unit is usable for a single test and can be recharged with chemicals for reuse. The main components of the Intoximeter are as follows (fig. 9): (1) a rubber balloon for initial collection and temporary storage of the breath sample; (2) a field test unit used as a screening test and consisting of a glass

tube containing a fritted glass disk charged with sulfuric acid and potassium permanganate, connected to the balloon; and (3) a quantitative test unit, consisting of a train of two tubes, containing respectively magnesium perchlorate and Ascarite.

The operations in the field consist of three steps: (1) collection of a sample of mixed expired breath by inflation of the rubber balloon; (2) passage of a small portion of the collected breath through the field test unit containing an acid potassium permanganate solution (a portion of any alcohol present in the breath reacts with the acid permanganate, destroying its original purple color in a time interval roughly inversely proportional to the breath alcohol [and therefore the blood alcohol] concentration); (3) successive passage of the remaining sample through the magnesium perchlorate tube and the preweighed Ascarite tube for later quantitative laboratory analysis. (The former tube quantitatively absorbs any alcohol and all water vapor present in the breath; the latter quantitatively absorbs the carbon dioxide.)

Fig. 8.—The Intoximeter.

After these initial steps the entire Intoximeter is returned to a suitably equipped laboratory, where the quantity of absorbed alcohol is distilled and determined by the Harger [5] or other suitable laboratory test and the Ascarite tube is reweighed, yielding the weight of carbon dioxide from the increase in weight over that before the test. From the analysis of alcohol and carbon dioxide, the blood alcohol concentration is calculated on the basis of the observation that the weight of alcohol

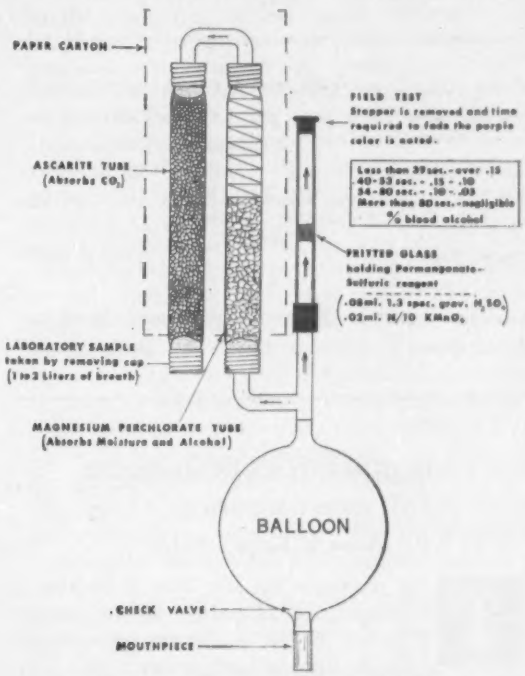

Fig. 9.—Schematic diagram of the Intoximeter.

present in 1 ml. of blood is equal to that accompanying 190 mg. of carbon dioxide in the mixed expired or alveolar breath.

Performance of the on-the-spot field test and breath collection usually requires about five minutes.

The Intoximeter Association has announced the development of a "photoelectric intoximeter" which is stated to employ an alveolar air sample and potassium dichromate in sulfuric acid solution as the oxidizing reagent for quantitative breath alcohol analysis and to incorporate provisions for the simultaneous collection of a second alveolar air sample for subsequent confirmatory laboratory analysis.

The bibliographic references have been omitted from THE JOURNAL and will be supplied, on request, by the Committee on Medicolegal Problems, 353 N. Dearborn St., Chicago 10.

The illustrations are used through the courtesy of the following persons or organizations: figure 1, Frederick G. Keyes, Inc.; figures 2, 4, 5, 7, and 9, Prof. R. F. Borkenstein, Indiana University; figure 3, Schueler and Co.; figure 6, the Stephenson Corporation; and figure 8, the Intoximeter Association.

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THE HUMANITIES IN MEDICINE

GUEST EDITORIAL

Amos R. Koontz, M.D.

THE physician has long been looked on as a special sort of person in our society. The best of the profession have always been leaders in their communities. The repute in which the physician has been held was eloquently stated in Robert Louis Stevenson's tribute to him: "He is the flower of our civilization, and when that stage of man is done with, only to be marveled at in history, he will be thought to have shared but little in the defects of the period and to have most notably exhibited the virtues of the race."

For generations the best of our physicians have been educated not only in the science of their times but also in the humanities. However, there was a time when some of our medical schools were "proprietary schools," which did not require even a grammar school education as a prerequisite to study medicine. About 50 years ago that deplorable situation changed as a result of the well-known Flexner report and the American Medical Association's simple device of classifying schools as A, B, and C schools. Many schools which could not stand the publicity of their lower classifications went out of existence, thus reducing the number by more than half. We now have standard minimal entrance requirements, and the general educational average of the entering student is far superior to what it had ever been before this change was made.

In spite of the better education offered today the comment is often heard that the medical manuscripts are dull and boresome in comparison to those of 50 years ago. Few physicians today write as Osler did. Welch's lectures were erudite and Lewellys F. Barker was gifted with a flow of English such as few people have attained. Other examples could be cited. What has caused the difference?

In some of our select medical societies, one hears prominent men use poor English and pronunciation so bad that the listener is distracted from the content of the paper. There are probably two reasons for this.

First, our secondary education has deteriorated, except in the best private schools and the exceptional public school. Superintendents of public instruction and school boards have required teachers to take courses (mostly repetitious) in education, in order to become "qualified" and to be advanced. The stress has been on method instead of content. Not only are some of these courses useless but they hinder the acquisition of a real education in such fundamentals as mathematics, history, the languages, and science. This trend has been carried over into our colleges, where, with the number of "snap" elective courses offered, it is possible to graduate and still be an ignoramus. This is not the fault of our youth but of the type of educational processes to which they are exposed.

Young persons who are going to study medicine must have a more serious outlook on educational problems than the average student. But many youngsters do not decide to study medicine until they are well along in college and often not until they are through. If they have not taken the solid courses and skipped the froth along the way, they will not be prepared for medicine.

About the time of World War I, "premedical" courses were instituted, to insure that those who were to study medicine would be properly grounded in the fundamental sciences they would need to understand the medical sciences. As time went on and competition for entrance to medical schools became keen, these courses "backfired," resulting in the average student entering medical school with a far more limited fundamental education than a physician should have. As medical schools stressed science in entrance requirements, the premedical student loaded up on science and often completely neglected the humanities. Some medical schools now (belatedly) are concerned about this and deplore that their entering students have not a well-rounded education. If physicians are to take the social and cultural positions in their communities which is the ideal of our profession, every one who is to study medicine should be liberally educated in both the sciences and the humanities. Once this is accomplished, medical schools need not

worry about the fundamental education of the students whom they select for admission, and the medical public need not worry about the diction of speakers at medical meetings or the lucidity of papers in medical journals.

In the meantime, we have on our hands a whole generation of physicians who entered medical school qualified in science but not in the humanities. Must such physicians sit and bemoan their fate? Certainly not. By properly selected reading, they can still broaden their education. But when is a practitioner, busy with patients, staff meetings, committee meetings, the medical literature, medical meetings, and writing papers, to have time for outside reading. The answer is utilization of scraps of time. There should always be nonmedical reading material on the bedside table. A few minutes to half an hour may be utilized before the lamp is turned off. A good book should be at hand when one is waiting for trains and planes and every overnight bag should contain one. And don't waste time looking out the window—grab a book. The more comprehensive a man's education, the better physician he will be. He is thereby given more of the human touch.

"In no profession does culture count for so much as in medicine, and no man needs it more than the general practitioner, working among all sorts and conditions of men, many of whom are influenced quite as much by his general ability, which they can appreciate, as by his learning of which they have no measure. The wider and freer a man's general education the better practitioner he is likely to be, particularly among the higher classes to whom the reassurance and sympathy of a cultivated gentleman of the type of Eryximachus, may mean much more than pills and potions." Osler said that.

CARDIAC RESUSCITATION IN MYOCARDIAL INFARCTION

Sudden death may occur in the early stage of acute myocardial infarction as a result of either ventricular standstill or ventricular fibrillation. A few such patients with recent myocardial infarction have been saved, where quick and heroic action together with fortunate circumstances were responsible for resuscitation with cardiac massage during the critical four-minute period.[1] It would seem that the time has come when a greater number of deaths from ventricular fibrillation or standstill could be prevented by planned readiness for such emergency resuscitation of patients admitted to the hospital with a diagnosis of recent myocardial infarction. Fortunately, in some patients with acute or impending myocardial infarction a warning develops in the form of bouts of premature beats or advanced atrioventricular block before the fatal change in cardiac mechanism sets in. Consideration should be given to placing patients in the acute stage of myocardial infarction routinely under continuous electrocardiographic observation with a monitoring system for excessive slowing or acceleration of the ventricular action; thus it might be possible both to recognize in time the patient who is in immediate danger of developing a fatal disturbance of cardiac rhythm and to foresee whether he is threatened by ventricular standstill or ventricular fibrillation. New methods for the treatment of the former have become available. An external pacemaker for electric stimulation of the heart [2] has been used successfully under such circumstances [3] and may now be replaced by the newly developed transistor pacemaker with percutaneous insertion of a myocardial electrode.[4] It is to be expected that a similar device, which would eliminate the need for thoracotomy, will be perfected for defibrillation of the ventricles, although rhythmic manual compression ("massage") may still be necessary in certain cases to restore and maintain pumping action until resumption of spontaneous coordinated heart action.

1. Nickel, S. N., and Gale, H. H.: Altered Prognosis with Cardiac Massage: Cardiac Resuscitation in Acute Myocardial Infarction—Report of Two Successfully Treated Cases, J. A. M. A. **170**:23-27 (May 2) 1959.

2. Zoll, P. M.: Resuscitation of Heart in Ventricular Standstill by External Electric Stimulation, New England J. Med. **247**:768-771 (Nov. 13) 1952.

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4. Thevenet, A.; Hodges, P. C.; and Lillehei, C. W.: Use of Myocardial Electrode Inserted Percutaneously for Control of Complete Atrioventricular Block by Artificial Pacemaker, Dis. Chest **34**:621-631 (Dec.) 1958.

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COUNCIL ON NATIONAL DEFENSE

ARMY MEDICAL SERVICE PRESENTS MASS CASUALTY CARE CONCEPTS AND TECHNIQUES

The seventh annual National Civil Defense Conference will be held in Atlantic City on Saturday, June 6, immediately prior to the opening of the annual American Medical Association convention.

"The one-day program will highlight medical problems involved in nuclear warfare," said Dr. Harold C. Lueth. "The program . . . will dramatize the important fact that the medical and health professions can take positive action to minimize the impact of mass casualties if properly trained and organized." Dr. Louis M. Orr will open the conference. Physicians attending the meeting will get a one-day version of the Army's one-week education and training program dealing with mass casualty concepts and treatment techniques.

The general methods of instruction for these courses include lectures, student participation, group and panel discussions, visual aids, and manikin demonstrations. Currently, the courses are being given at Walter Reed Army Medical Center in Washington, D. C., and Brooke Army Medical Center in San Antonio, Texas. The courses embrace both the short-term and long-term expected injuries. Counter medical and health measures are stressed to combat the nuclear effects of blast, burn, and radiation injuries, both from the preventive and curative standpoint. All information pertaining to registration may be obtained from Frank W. Barton, Secretary, Council on National Defense, American Medical Association, 535 N. Dearborn St., Chicago 10.

Morning

8:00-9:00 Registration

9:00-9:05 **Call to Order and Introductory Remarks**
HAROLD C. LUETH, M.D., Chairman, Committee on Disaster Medical Care, Council on National Defense, A. M. A.; Member, Council on National Defense, A. M. A., Evanston, Ill.

9:05-9:15 **Welcome Address on Behalf of A. M. A.**
LOUIS M. ORR, M.D., President-Elect, A. M. A., Orlando, Fla.

9:15-9:25 **Introduction to Army Medical Service Course on Management of Mass Casualties**
The Surgeon General, Department of the Army.

9:25-9:40 **Graphic Presentation of Situation**

9:40-10:10 **Casualty Estimation and Analysis**
Major JACK C. FITZPATRICK, MC, USA, Nuclear Medical Officer, Office of the Assistant for Nuclear Warfare, Instruction and Casualty Studies, Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, Texas.

10:10-10:45 **Casualty Demonstration**
Lieut. Col. VINCENT I. HACK, MSC, USA, Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, Texas.

10:45-11:00 BREAK

11:00-11:20 **First Aid: Survival Care**
Lieut. Col. JOSEPH D. GOLDSTEIN, MC, USA, Chief, Department of Atomic Casualties Studies, Walter Reed Army Institute of Research, Washington, D. C.

11:20-11:30 **Discussion of Emergency Medical Packet for 100 Casualties**
Col. THEODORE M. CAROW, MC, USA, Chief, Supply Division, Office of the Surgeon General, Department of the Army, Washington, D. C.

11:30-12:00 **Sorting and Establishment of Priorities**
Lieut. Col. H. HASKELL ZIPERMAN, MC, USA, Director, Department of Military Medicine and Surgery, Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, Texas.

Afternoon

12:00-12:30 **Management of Burns Resulting from Nuclear Disaster**
Lieut. Col. EDWARD H. VOGEL, MC, USA, Commanding Officer, Surgical Research Unit, Brooke Army Medical Center, Fort Sam Houston, Texas.

12:30-1:00 **Management of Soft Tissue Trauma**
Lieut. Col. WILLIAM H. MONCRIEF JR., MC, USA, Director, Division of Surgery, Walter Reed Army Institute of Research, Washington, D. C.

1:00-2:15 LUNCH

2:15-2:45 **Preventive Medicine in Disaster: Public Health Aspects**
Col. PHILIP R. BECKJORD, MC, USA, Assistant Chief, Preventive Medicine Division, Office of the Surgeon General, Department of the Army, Washington, D. C.

2:45-3:15 **Chemical and Biological Warfare**
Col. WILLIAM D. TIGERTT, MC, USA, Commanding Officer, United States Army Medical Unit, Fort Detrick, Md.

3:15-3:30 BREAK

3:30-3:45 **Impact of Radioactive Fall-out on Medical Operations**
Col. ROY D. MAXWELL, MSC, USA, Assistant for Nuclear Warfare Instruction and Casualty Studies, Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, Texas.

3:45-4:15 **Psychological Aspects of Disaster**
Col. ALBERT J. GLASS, MC, USA, Chief Psychiatry and Neurology Consultant, Office of the Surgeon General, Department of the Army, Washington, D. C.

4:15-5:00 **Panel Discussion—Question Period**

MEDICAL NEWS

ALASKA

Rise in Radioactivity.—During the first six weeks of 1959 air sampling stations at Juneau, Anchorage, and Fairbanks all measured radioactivity, which rose to about 10 micromicrocuries per cubic meter of air according to reports received by March 1 at the Alaska Department of Health radiological office in Juneau. When the first monitoring station of Alaska's radiation surveillance network went into operation at Juneau in May, 1956, the background radioactivity was measured at 0.15 to 0.25 micromicrocurie per cubic meter of air. The highs recorded in Juneau between Jan. 1 and Feb. 17, were 11.4 on Jan. 5, 5.9 on Jan. 26, and 9.3 on Feb. 9. In Anchorage the reading on Jan. 16 was 7.6, after which it went up to 8.7 on Jan. 23 and 9.2 on Jan. 26. In Fairbanks the highest reading for the period was 10.5 on Jan. 26. The readings are the USPHS Washington laboratory results obtained from 24-hour air samples made in Alaska by using 4-inch dust filters and indicating beta activity in comparison with a 0.02 microcurie radioactive strontium standard.

CALIFORNIA

Program for Teaching and Research.—Under a $255,000 grant from the Russell Sage Foundation, Stanford Medical School will establish a new teaching and research program that combines social sciences with medicine. Students and faculty of the Medical School and of the departments of sociology, psychology, and anthropology will collaborate. The program will begin next fall when the medical school moves into its new 20-million-dollar center on the campus. The Russell Sage grant will provide basic support for the first five years. It will finance a beginning staff, student fellowships, and research. Nurses, social workers, and other members of the health team are expected to join the program eventually. Plans were developed from studies supported by an earlier grant from the foundation. The planners included Associate Dean Lyman M. Stowe of the Medical School, and professors Rodney R. Beard, of preventive medicine, Thomas A. Gonda, of psychiatry, and Edmund H. Volkart, Ph.D., of sociology. Professor Volkart will direct the program during its first year. It will emphasize interdepartmental teaching and research and will supplement health teaching and research along current lines.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Chicago

Annual I. F. Volini Lectureship.—This lectureship, presented annually under the auspices of the Phi Sigma of Phi Chi, of which fraternity Dr. Volini was a member, was given April 6 by Dr. Edward Compere, Northwestern University Medical School, on "The Stimulation or Retardation of Bone Growth."

English Anatomist to Lecture.—The 1959 Solomon Theron De Lee Lecture will be given by Prof. Sir Solly Zuckerman, C.B., F.R.S., department of anatomy, The Medical School, The University of Birmingham, England, on "The Control of the Gonadotrophic Functions of the Pituitary" in Dora De Lee Hall, The Chicago Lying-In Hospital, University of Chicago, 5841 Maryland Ave., Thursday, May 7, 4:30 p. m.

University News.—Dr. Andre Michel Lwoff, French authority on microbiology, presented a medical lecture at the University of Chicago entitled "Factors Influencing the Evolution of Viral Diseases at the Cellular Level in the Organism," sponsored by the E. R. Squibb and Sons Centennial Lecture Program. Dr. Lwoff has been with the Pasteur Institute, Paris, since 1921 and has been head of the department of microbial physiology since 1938.

Dr. Hasegawa to Receive Fellowship.—Dr. Junji Hasegawa has been named to receive the 1959 Gillette–Toni Fellowship for dermatologic study at the Northwestern University Medical School. This is the second straight year Dr. Hasegawa has been honored with this award by the fellowship committee at Northwestern. He will conduct research in dermatology under the direction of Dr. Herbert Rattner, chairman of the school's dermatology department. The fellowship grant totals $4,000, of which $2,500 is paid to Dr. Hasegawa with an additional $1,500 given to the university to defray tuition and departmental overhead expenses.

Break Ground for Diagnostic Center.—Groundbreaking ceremonies for a $1,980,000 Diagnostic Center Building at University of Chicago Clinics were held April 14. The new building, to be located at 59th Street and Drexel Avenue, will provide a central location to serve the 200,000 outpatient visitors to the clinics each year. The Diagnostic Center Building will be accessible to the Univer-

sity of Chicago hospital group's 36 clinical areas. Maurice Goldblatt, chairman of the University of Chicago Cancer Research Foundation, and John I. Kirkpatrick, vice-chancellor of the University of Chicago, gave addresses at the ceremonies, after which Dr. Lowell T. Coggeshall, dean of the division of biological sciences of the University of Chicago, spoke at a luncheon.

Lectures on Surgical History.—Two lectures on surgical history will be presented at the International College of Surgeons Hall of Fame on May 5. Dr. Francis L. Lederer, head, department of otolaryngology, University of Illinois College of Medicine, will speak on "The Evolution of Otorhinolaryngology and Bronchoesophagology." Dr. Wayne B. Slaughter, chairman and professor in charge of plastic surgery, University of Wisconsin, Madison, and Stritch School of Medicine, Loyola University, will speak on "The History of Plastic Surgery." The lectures are open to physicians, medical personnel, and the public. Information may be had by writing Dr. Ross T. McIntire, Executive Director, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

INDIANA

Surgeons Meeting in Indianapolis.—The Indiana Division, U. S. Section, International College of Surgeons, will hold its annual regent's meeting at the Indiana University Medical Center, Indianapolis, May 6. Papers to be presented include "Indications for Surgery of Peptic Ulcer, and Surgical Procedures Advised," by Dr. Claude J. Hunt, Kansas City, Mo., and "Types of Colostomies and Indications," by Dr. Peter A. Rosi, professor of surgery, Cook County Graduate School, and associate professor, Northwestern University, Chicago. The banquet at the Sheraton–Lincoln Hotel (Travertine Room) will be highlighted by a talk on "Sputniks, Space, and You" by Robert J. Dryter, consulting engineer. All surgeons, medical practitioners, their ladies, and guests are invited. For information write Dr. Simon Reisler, 318 Bankers Trust Bldg., Indianapolis.

KENTUCKY

Physicians Over 85 Still Active.—Four physicians, all over 85 years of age, are still actively practicing medicine in Morganfield. Combined they have a total of 223 years of medical experience. They are Dr. John W. Conway, who has had 60 years of experience; Dr. Henry B. Allen, who has practiced 56 years; Dr. Casey B. Graves, who has practiced 54 years; and Dr. Herbert B. Stewart, 53 years.

Dr. Parker to Come to Lexington.—Dr. Joseph B. Parker Jr., associate professor of psychiatry, Duke University Medical Center, Durham, N. C., has been named psychiatry department chairman for the University of Kentucky's new medical center in Lexington. He will be professor of psychiatry and will assume his new duties late next summer. Dr. Parker is chief of psychiatric service at the Veterans Administration Hospital, Durham, N. C. Associated with Duke University since 1953, he was a member of the University of Tennessee psychiatry faculty from 1949-53. His major research interest is in the field of manic-depressive reactions. Dr. Parker recently was elected a member of the American Psychopathological Association. He is a fellow of the American Psychiatric Association and the Southeastern Psychiatric Association. His professional activities include service as director of postgraduate refresher courses in neuropsychiatry for the Southeastern Area of the Veterans Administration.

MASSACHUSETTS

New Research Training Program.—A new training program for medical researchers has been announced jointly by officials of the New England Center Hospital and the Massachusetts Institute of Technology. A grant has been made by the National Heart Institute, National Institutes of Health, to the New England Center Hospital, which includes the Pratt Diagnostic Clinic, to establish a three-year training program in cooperation with M. I. T. for clinical scientists in cardiovascular and pulmonary research. The grant will be under the direction of Dr. Samuel Proger, physician-in-chief, New England Center Hospital, and professor of medicine, Tufts University School of Medicine. In direct supervision will be Dr. Leon Cander who heads the hospital's pulmonary physiology laboratories. The program was developed by Dr. Cander in conjunction with Irwin W. Sizer, Ph.D., chairman, department of biology at M. I. T. As planned, the program will provide for the trainees to spend the first year of study as special graduate students at M. I. T., taking courses in advanced mathematics, physical chemistry, instrumentation, and other subjects applicable to their expected field of investigation. Their second year will be spent in special medical postgraduate studies at the New England Center Hospital and will include special graduate courses at M. I. T. In the third and final year each trainee will be encouraged to involve himself in a field of special investigation interest, spending his time in the Ziskind Research Laboratories of the New England Center Hospital and at M. I. T. for additional appropriate courses. For information, write the New England Medical Center, 37 Bennet St., Boston 11.

Projects to Reduce Mental Hospital Admissions.—Two research projects to reduce the number of in-patient admissions to mental hospitals, involving the use of psychiatric home treatment and a study of alternatives to hospitalization for geriatric patients, are underway at the Boston University

School of Medicine and Boston State Hospital. Both programs are supported by grants from the U. S. Department of Health, Education, and Welfare, Public Health Service, National Institute of Mental Health, and are under the direction of Dr. Walter E. Barton, of Boston, associate professor of psychiatry and superintendent of the hospital. Two teams, each consisting of a doctor, a psychiatric social worker, and a psychiatric nurse, working on the home-care project, are working in the Dorchester area of Boston, a community with 100,000 inhabitants who belong, predominantly, to the middle and lower class groups with mixed ethnic and religious backgrounds. The doctors use psychotherapy as their primary tool, as they would if they were seeing the patient in their office or an out-patient clinic. The geriatric project is being done in two stages. The first involves extensive interviews of 75 geriatric patients admitted to the hospital, their families, friends, and associates, to get as complete a picture as possible of the needs of older people, where in their lives they failed to provide for these needs, and what can be done to maintain these people in their home surroundings. The second step will involve interpretation of data to see what types of community resources are needed to allow these people to remain in their home communities, instead of admitting them to mental hospitals.

MICHIGAN

Campaign for Atomic Research Project.—The University of Michigan has launched a campaign to raise 2 million dollars for its Memorial–Phoenix Project for atomic research. At a meeting of 104 state business and industrial leaders April 1, James C. Zeder, Chrysler Corporation vice-president and campaign committee chairman, said that funds raised to establish the project in 1948 as a memorial to the university's World War II dead are nearly exhausted. A total of 8 million dollars was contributed by university students, alumni, friends, and industrial groups to start the Phoenix Project. The money has been used to build a million-watt nuclear reactor and research facilities, to support 185 research projects, to buy equipment, to free scientists for full-time investigations, and to provide information about the atomic energy field. The Phoenix Project reportedly "is the largest independent atomic research program in the world. It operates the nation's most powerful college nuclear reactor, has brought about the country's largest enrollment in nuclear engineering and science at the U-M, and has sent people to help 20 other nations set up their own peaceful A-energy programs."

Hold Open House for New Buildings.—Exhibits and demonstrations, ranging from monkey morphine addicts to laboratory research on individual cells, were displayed Feb. 22 when the University of Michigan Medical Center, Ann Arbor, held community "open house" in the new 8½-million-dollar buildings of the Medical School and School of Nursing. Over 25 exhibits were manned by faculty members of the various departments to give visitors a firsthand picture of the training and research activities. The Medical Sciences Building opened last fall and houses the departments of biological chemistry, pathology, and pharmacology. Located at the northwest corner of the Medical Center, the structure is the fifth building occupied by the Medical School since its establishment 109 years ago. Biochemists displayed a research laboratory in full operation, and pathologists opened their tissue laboratory. In the pharmacology department, visitors saw some of the 250 Indian macaca monkeys which are used in studying narcotic addiction. At the School of Nursing demonstrations of modern nursing care were given. A cancer display, a newly developed germ-free laboratory, and an apparatus which charts the effect of different drugs on a living turtle heart were featured. The new home of the Medical School consists of three interconnecting buildings linked to the University Hospital by an enclosed bridge. It contains over 123,000 square feet of teaching, research, and office space, including the administrative quarters of the two schools. The first medical building was erected in 1850 on the east side of the main campus at a cost of $9,991. In 1903, West Medical opened at a cost of $137,000 and this was followed in 1936 by East Medical, built at a cost of $858,283. Future plans call for a 9-million-dollar addition to the new Medical Sciences Building. This will be joined to the west end of the new structure and will provide space for the departments of anatomy, physiology, and bacteriology which are located in East Medical.

MISSISSIPPI

Annual State Meeting in Biloxi.—The Mississippi State Medical Association will hold its 91st annual session at the Hotel Buena Vista, May 12-14, under the presidency of Dr. Guy T. Vise, Meridian. Six section meetings will be held and the surgery section will include a panel on "Technical Mishaps Occurring During Surgery: Recognition and Management," moderated by Dr. James D. Hardy, Jackson. Dr. Louis M. Orr, Orlando, Fla., President-Elect, American Medical Association, will participate in the program, which lists the following essayists: Drs. A. Frank Adair Jr., St. Paul, Minn.; Jack R. Anderson, John Perrigo Fox, Ralph V. Platou, and Lewis J. Rutledge, New Orleans; James H. Ferguson, Miami, Fla.; Benjamin R. Gendel, Atlanta, Ga.; Phil C. Schreier and Alva B. Weir Jr., Memphis, Tenn.; and Edward R. Woodward, Gainesville, Fla. Scientific and technical exhibits are planned. Activities include a golf tournament and skeet shoot, May 13. For information write Mr. R. B. Kennedy, 735 Riverside Dr., Jackson, Miss., Executive-Secretary.

MISSOURI

Student Gets Research Fellowship.—John R. Esther, who last June finished his second year in medicine at the University of Missouri School of Medicine, Columbia, has received a postsophomore fellowship in pathology from the National Institutes of Health, Bethesda, Md., to study ways to predict in the unborn child the severity of an infant disease caused by parental differences in the Rh factor. He is now working full time on his research in the department of pathology at the Medical Center, under the direction of Dr. Joseph E. Flynn, chairman, department of pathology, and Dr. Vincent P. Perna, assistant professor of pathology. Mr. Esther is recorded as the first student in the history of the School of Medicine to be awarded a postsophomore fellowship by the National Institutes of Health of the U. S. Public Health Service.

NEW JERSEY

Conference on Mental Retardation.—The second annual Spring Conference of the Training School of Vineland will be held May 11-12, on the subject "Practical Problems" of coordinating and integrating all services related to the treatment, training, and management of the mentally retarded. Sponsors of the conference are the Training School and the New Jersey Department of Institutions and Agencies. The conference was developed under a grant from the National Institute of Mental Health. The clinical areas of psychiatry, psychology, education, speech and hearing, medicine, social work, and daily care will be represented. The conference goal is to produce a set of written, specific, desirable practices of coordinating and integrating information which can be used by workers in schools, institutions, clinics, other agencies and private practice. The conference is composed of panels and subworkshops, with representatives from the seven clinical areas represented in each. Two lectures will be presented: "Diagnosis . . . Original and Continuing," by Dr. Margaret J. Giannini, administrative director, Mental Retardation Clinic, New York Medical College; and "Recommendations by Clinicians," by Dr. William P. Hurder, of Atlanta, Ga., assistant director for mental health, Southern Regional Education Board. For information write Walter Jacob, Ph.D., Director, The Training School, Vineland, N. J.

NEW YORK

Dr. Lotspeich to Come to Rochester.—Dr. William D. Lotspeich, chairman, physiology department, University of Cincinnati College of Medicine, since 1951, will come to the University of Rochester School of Medicine and Dentistry as chairman of its department of physiology. Dr. Lotspeich will begin his new duties at the Medical School July 1, succeeding Wallace O. Fenn, Ph.D., who has headed the department since 1924. Dr. Fenn is retiring from the chairmanship but will continue as professor of physiology. Dr. Lotspeich is also Joseph Eichberg Professor of Physiology. After serving as instructor and assistant professor in physiology at Syracuse University College of Medicine from 1947 to 1949, Dr. Lotspeich spent two years as a research fellow in biochemistry at Oxford University, England, where he worked on tissue metabolism with Sir Rudolph Peters. He is a member of the Physiological Study Section of the National Institutes of Health, U. S. Public Health Service, and of the Advisory Council, Life Insurance Medical Research Fund of New York.

New York City

City Hospital Restores Name.—New York City's new municipal hospital, known for a brief time as Elmhurst General Hospital, has had restored to it its former name of City Hospital. Founded in 1832, it has a bed capacity of 1,066 and serves as the municipal hospital for half the borough of Queens, which now comprises two million people.

Lecture on Radiation Therapy.—The Radiation Therapy Alumni Association of Bellevue Hospital announced that the eighth annual Ira I. Kaplan Lecture, "Megavoltage X-Ray Therapy," will be given by Dr. John W. Boland, director of radiotherapy, Mt. Sinai Hospital, on May 7, 5:30 p. m., at the New York University Bellevue Medical Center, 31st Street and First Avenue, Founders Hall.

Establish Annual Fried Lecture.—Patients of Dr. Boris M. Fried have established an annual lecture at New York Medical College in his honor to be known as the Dr. B. M. Fried Lecture. The first address was given March 13. Wendell J. Krieg, Ph.D., professor of anatomy, Northwestern University Medical School, Chicago, was the speaker. Dr. Fried, clinical associate in the department of medicine at New York Medical College, has served on the staff of the department of pathology, Harvard Medical School, and has done experimental pathology at the Peter Bent Brigham Hospital, Boston. Later he was a research fellow in pathology at Mount Sinai Hospital.

Dr. Loeb Receives Kober Medal.—Dr. Robert F. Loeb, professor of medicine, Columbia University, since 1938, has been awarded the Kober Medal for 1959. The medal is provided for by the Kober Foundation, established at Georgetown University, Washington, D. C., in 1923. Dr. Loeb was selected for this year's medal by the Association of American Physicians "in recognition of his contributions to the progress of the medical sciences." He will receive the award at the association's annual meeting in Atlantic City in May. Dr. Loeb, who holds honorary doctorate degrees from the Universities of Chicago, Paris, Strasbourg, and Wales, was Lambert

Professor of Medicine at Columbia from 1942 to 1947 and has been Bard Professor of Medicine there since 1947. The award of the Kober Medal is provided for by an endowment fund established in 1923 by Dr. George M. Kober to commemorate the 50th anniversary of his graduation in medicine from Georgetown. The fund also pays the expenses of an annual lecture on a medical subject, a scholarship in the Georgetown Medical School, and a gold medal "to be awarded to the best student in hygiene."

Exhibit of Books on Physicians.—On view at The New York Academy of Medicine is an exhibit entitled "Books About Physicians" devoted to literary contributions by physicians and about medical life. In the category devoted to the physician in fiction is a copy of Sinclair Lewis' "Arrowsmith," deposited in the Library by Paul De Kruif, Ph.D., who collaborated on the work. One exhibit case is devoted to Dr. Hans H. Zinsser, a native New Yorker, who for many years held the chair of bacteriology and immunology in the College of Physicians and Surgeons and was later appointed to a similar chair in the Harvard University Medical School, Boston. He was distinguished as a teacher, investigator, literary man, and poet. Three cases are devoted to physicians and medicine as portrayed in fiction and drama, from the works of Rabelais to Doctor Zhivago. There are medical essays of distinguished physicians, such as Maimonides of the 12th century and Oliver Wendell Holmes of the 19th. Medicine's modern poets Merrill Moore and William Carlos Williams are represented. A number of autobiographies by medical men are exhibited. Other cases hold narratives of medical missionaries and a wide variety of contributions shown in anthologies. The exhibit will be on display in the library through June 30.

PENNSYLVANIA

Industrial Scientists Honored.—Dr. Karl H. Beyer Jr. and James M. Sprague, Ph.D., of West Point, will receive the Merck Board of Directors' Scientific Award for scientific accomplishments. A means of honoring industrial scientists, the award takes the form of an appropriate scroll setting forth the scientist's achievements and a grant of funds by Merck to one or more educational institutions to support an appropriate educational activity in the scientist's name. The institution is chosen by the recipient and the type of educational activity is developed by the recipient and the university. In honor of Dr. Beyer, the Merck board is granting $25,000 to the University of Wisconsin to establish the Karl H. Beyer Jr. Visiting Professorship in the university's School of Medicine. Of the $25,000 appropriated in honor of Dr. Sprague, the board is granting $10,000 to Franklin College (Franklin, Ind.) to set up the James M. Sprague Science Award, to provide financial assistance to "exceptionally able" students in natural science. The sum of $15,000 is being granted to the University of Wisconsin to establish the James M. Sprague Fund to be used by the university's department of chemistry for a visiting lectureship in organic chemistry, the James M. Sprague Lectureship. The Directors' Scientific Award was established by the Merck Board in 1951 at the suggestion of former company president James J. Kerrigan. These awards now support the Karl Folkers Lecture Series in Chemistry at the Universities of Illinois and Wisconsin, the Lewis Hastings Sarett Scholarship in Chemistry at Northwestern and Princeton Universities, the Max Tishler Prize Scholarship at Tufts College, and the Max Tishler Lectures in Chemistry at Harvard University.

Philadelphia

Foreign Visitors.—The University of Pennsylvania School of Medicine's department of psychiatry was visited by five foreign psychiatrists at a special round-table conference on psychiatric education March 23. The visitors included Dr. Hans Hoff, chairman, department of psychiatry, University of Vienna; Dr. Pierre Deniker, senior lecturer, University of Paris; Dr. Roland Kuhn, professor of psychiatry, University of Zurich; Dr. Michael Shepherd, department of psychiatry, University of London; and Dr. Hanns Hippius, department of psychiatry, University of Berlin.

Personal.—Dr. Albert P. Seltzer has been appointed as senior attending otolaryngologist to the Albert Einstein Medical Center, Southern Division, Philadelphia.—Dr. Edward L. Bortz, formerly president of the American Medical Association, and now chief, medical service, the Lankenau Hospital, Philadelphia, was named chairman of the 1960 National Health Forum. The forum, an annual national conference, is sponsored by the National Health Council on behalf of its more than 60 member agencies.—Dr. C. Wilmer Wirts, associate professor of medicine, Jefferson Medical College, was awarded a scroll March 18 in recognition of his service rendered during his three-year term (1957-59) as director of the Postgraduate Institute of the Philadelphia County Medical Society.

Undergraduate Education Via Television.—An experiment linking five major medical schools by closed-circuit TV was held March 31-April 10. Joining in this network for undergraduate medical education were the University of Pennsylvania School of Medicine, Jefferson Medical College, Temple University School of Medicine, Hahnemann Medical College, and Woman's Medical College of Pennsylvania. The programs were produced by the Medical Education Service Unit of Smith Kline & French Laboratories, Philadelphia. The special telecasts, a

series of five lectures by Dr. Joseph W. Spelman, medical examiner for the City of Philadelphia, reportedly marked the first time that five medical schools used the technique of television for joint lecture-demonstration purposes. About 1,300 students in selected classes of the schools watched the color telecasts on screens as large as 4½-by-6 feet in their own auditoriums. The series of 45-minute programs was arranged under the subject, "Forensic Medicine." A telephone hook-up was used to relay the students' questions directly to Dr. Spelman through a moderator at each of the schools. The idea for the lecture series grew out of talks between Dr. Charles S. Cameron, dean of Hahnemann Medical College, and officials at Smith Kline & French.

SOUTH CAROLINA

Annual Meeting in Columbia.—The South Carolina Medical Association will hold its annual meeting in Columbia, May 13-14. Two panel discussions are planned on (1) cancer, and (2) vascular disease, moderated by Dr. Harold R. Pratt-Thomas and Dr. Robert Wilson, Charleston, respectively. The following papers will be presented by out-of-state speakers:

Doctor Looks at the Problem of Radiation Hazards, Dr. Eugene P. Pendergrass, Philadelphia.
Advances in Cancer Control, Dr. John R. Heller, Bethesda, Md.
Fenestration Operation on Ear, Dr. J. Brown Farrior, Tampa, Fla.
Some Pediatric Orthopedic Problems, Dr. William T. Green, Boston.
Vesicoureteral Reflux in Children: Diagnosis and Management, Dr. Victor A. Politano, Durham, N. C.
Problems in Staphylococcus Infection, Dr. Walter A. Murray, Columbus, Ohio.

A Clinicopathologic conference is scheduled for the afternoon of May 14. Speaker at the annual banquet that evening will be Dr. Gunnar Gundersen, La Crosse, Wis., President, American Medical Association. For information write Mr. M. L. Meadors, 309 W. Evans St., Florence, S. C.

TENNESSEE

Society Elections.—The Tennessee State Orthopaedic Society held its 11th annual meeting at the University of Tennessee College of Medicine March 15. Dr. George W. Shelton was elected president; Dr. W. Houston Price, vice-president; Dr. Maurice A. Canon, secretary-treasurer. The 1960 meeting will be held in Chattanooga.—The following are officers of the Nashville Academy of Medicine for 1959: president, Dr. Rollin A. Daniel Jr., and secretary-treasurer, Dr. Douglas H. Riddell, 2318 W. End Ave., Nashville 5, Tenn.

Name Dr. Zilversmit Heart Investigator.—Donald Zilversmit, Ph.D., professor of physiology, University of Tennessee, Memphis, was named the seventh "Career Investigator" of the American Heart Association. Career investigators are "outstanding scientists" who receive support from the American Heart Association throughout their productive lives. In his studies Dutch-born Dr. Zilversmit has concentrated on the body's use of lipids. The investigatorship provides $30,000 annually to cover the investigator's salary and to help underwrite the expenses of his laboratory. Its purpose is to relieve leading investigators of financial and other pressures and permit them to work without interruption on problems of their own choosing.

Personal.—Dr. Frank L. Roberts, associate dean, University of Tennessee College of Medicine, Memphis, will go to Iran for two years as a consultant in medical education of the University of Shiraz, an English-speaking university in southern Iran under auspices of the International Cooperation Administration.—Thomas P. Nash Jr., Ph.D., professor of chemistry and dean of the School of Biological Sciences, University of Tennessee Medical Units, Memphis, has won the 1958 Southern Chemist Award of the American Chemical Society's Memphis Section. The gold medal, given annually "for distinguished service to the profession of chemistry in the Southern states," was presented to Dr. Nash at a banquet at the University of Florida Dec. 12.

Dr. Rogers Named Department Head.—Dr. David E. Rogers, associate professor of medicine and chief of the division of infectious disease, New York Hospital, Cornell Medical Center, was named professor of medicine and head of that department at Vanderbilt University School of Medicine, Nashville. Dr. Rogers, whose appointment will take effect at the beginning of the 1959-1960 academic year, succeeds Dr. Hugh J. Morgan, who retired last June. Since June the department has been directed by a committee, with Dr. Rudolph H. Kampmeier as chairman. Dr. Rogers was appointed assistant professor of medicine on the New York Hospital–Cornell faculty in 1954, spent the following year as visiting investigator at the Rockefeller Institute for Medical Research, was made chief of the division of infectious disease in 1955, and was promoted to associate professor in 1956.

UTAH

Dr. Scott M. Smith Honored.—Dr. Scott M. Smith, of Salt Lake City, received the citation of merit award from the University of Missouri Alumni Association April 7. The presentation was made at the Medical School Alumni luncheon in connection with the Missouri State Medical Association meeting. Dr. Smith, associate clinical professor, department of anesthesiology, University of Utah College of Medicine, was elected president of the American Board of Anesthesiology in 1958 and has been a

board member since 1950. He was president of the American Society of Anesthesiologists in 1956, and became secretary of the American Academy of Anesthesiology in 1957. In the American Medical Association he was chairman of the section on anesthesiology in 1957 and for eight years was representative to scientific exhibits on anesthesiology.

VERMONT

Iranian Visitor.—Dr. Sh. Mofidi, professor, University of Teheran, Iran, was a visitor at the University of Vermont College of Medicine, Burlington, recently, observing the teaching of preventive medicine and discussing the problems of selecting and evaluating students for admission to medical school. Dr. Mofidi returned a visit to Iran made by Dean George A. Wolf Jr. last summer.

VIRGINIA

Dr. Paquin Comes to Charlottesville.—Dr. Albert J. Paquin Jr. was appointed professor of urology and chairman of the department of urology, University of Virginia School of Medicine, Charlottesville, effective May 1. Dr. Hugh Warren, associate professor of urology, has served as acting chairman of the department since the death of Dr. Samuel A. Vest Jr. last April. Dr. Paquin comes to the University of Virginia from Cornell University Medical College, New York City, where he was associate professor of clinical surgery and urology since July 1, 1957, and associate attending surgeon in urology at the New York Hospital–Cornell Medical Center. Dr. Paquin's interests have centered on the urological problems of childhood and the metabolic derangement induced by surgical trauma. He plans to continue this research.

Annual General Practice Meeting.—The ninth annual scientific assembly of the Virginia Academy of General Practice will be held May 7-10 at the Jefferson Hotel, Richmond. The morning of May 8 will be devoted to a program of the Virginia Diabetes Clinical Society and that afternoon the annual business meeting will be held. The following papers will be presented by out-of-state speakers:

Early Diagnosis of Uterine Cancer, Dr. C. Bernard Brack, Baltimore.

The Hirsute Female, Dr. Robert B. Greenblatt, Augusta, Ga.

Some Problems in Geriatric Medicine, Dr. Edward Henderson, Montclair, N. J.

The Child Handicapped by Nephrosis, Dr. Milton Rapoport, Philadelphia.

The Child Handicapped by Cerebral Palsy, Dr. George G. Deaver, New York City.

Man in Space, Capt. W. M. Snowden, Washington, D. C.

Therapeutically Induced Weight Gains in Hypertensives, Dr. Harold Feldman, Livingston, N. J.

Newer Concepts in the Treatment of Common Skin Diseases, Dr. Edmund F. Finnerty Jr., Boston.

Present Status of Adrenocortical Steroid Therapy, Dr. Nicholas E. Capeci, West Point, Pa.

Treatment of Hypertension, Dr. Francis L. Chamberlain, San Francisco.

Two motion pictures will be shown and exhibits are planned. Guest speaker at the annual banquet May 9, 7:30 p. m., will be Mr. T. Coleman Andrews, of Richmond, who will present "Wasteful Spending, Confiscatory Taxation and Inflation Are Not Laughing Matters." For information write the Virginia Academy of General Practice, 4205 Dover Road, Richmond 21, Va.

WASHINGTON

Appoint English Microbiologist as Laboratory Chief.—Dr. John C. Sherris, of Manchester, England, a member of the University of Manchester faculty, has been appointed chief of the Microbiology Laboratory of the University of Washington Teaching and Research Hospital, Seattle. Dr. Sherris, a graduate of Middlesex Hospital Medical School of London University, received his bachelor of medicine and bachelor of science degrees in 1948 and his doctor of medicine degree in 1950. He has been senior lecturer in bacteriology at the University of Manchester since 1956. Dr. Sherris' research has been in the application of experimental methods to problems in the diagnosis, treatment, and prevention of infectious disease in man.

WISCONSIN

Dr. Evans to Head New Department.—Dr. Alfred S. Evans, who for the past six years has been director of the Preventive Medicine Section of Student Health and associate professor of medical microbiology, University of Wisconsin Medical Center, Madison, has recently been appointed chairman of the newly established department of preventive medicine at the center and director of the State Laboratory of Hygiene. To develop a "broad and vigorous program" in preventive medicine and public health, the department has been completely divorced from the student health program and its educational and research activities merged with the program of the state Laboratory of Hygiene. However, the Laboratory of Hygiene shall continue to function as a separate unit—with Dr. Evans heading both departments. Dr. Evans has been associated with the University of Wisconsin Medical Center since 1952 and has held various positions on the staff of Yale University, New Haven, Conn. Dr. Evans will replace retiring Dr. William D. Stovall as director of the state Laboratory of Hygiene. Dr. Stovall, who headed the program for over 30 years, has agreed to stay on as acting director until Sept. 1 to allow Dr. Evans to study epidemiology and public health at the University of Michigan School of Public Health.

GENERAL

Travel Grants for Goiter Conference.—The fourth International Goiter Conference will be held July 5-9, 1960, in London, England, under the auspices of the London Thyroid Club and the American Goiter Association. The American Goiter Association plans to make available "to worthy candidates" a limited number of travel grants for participants of this meeting. Application blanks are available from Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., U. S. A. Applications will be received until Jan. 1, 1960.

Dr. Smith Goes to Washington.—The Pharmaceutical Manufacturers Association named Dr. Austin Smith, former editor of THE JOURNAL as its first full-time salaried president following a year of presidency of George F. Smith, who served as the first president after the 1958 merger combining the American Drug Manufacturers Association and the American Pharmaceutical Manufacturers Association. Dr. Smith will be located at PMA's Washington headquarters. Since 1953 he has been executive editor of the *World Medical Journal* and since 1954 has served as chairman of the board of the U. S. Committee, World Medical Association.

Otoophthalmological Meeting in Las Vegas.—The Pacific Coast Oto-Ophthalmological Society's annual meeting will be held May 3-7 at the Hotel Riveria, Las Vegas, Nev. Guest speakers will include: Drs. Robert R. Newell, San Francisco; William P. Mikkelsen, Los Angeles; James F. Crow, Ph.D., Madison, Wis.; Stuart C. Cullen, San Francisco; George E. Shambaugh Jr., Chicago; Sidney Riegelman, Ph.D., San Francisco; Lawrence R. Boies, Minneapolis; Dean M. Lierle, Iowa City; A. Edward Maumenee, Baltimore; John W. Henderson, Rochester, Minn.; and Morton D. Leigh, Los Angeles. The social events committee has planned programing for the members and their wives during the meeting. The President's Reception and Buffet Supper will be held Sunday evening, May 3. For information write Dr. Homer E. Smith, 686 Twelfth Ave., Salt Lake City 3, Utah, Executive Secretary-Treasurer.

Annual Psychosomatic Meeting.—The American Psychosomatic Society's 16th annual meeting will be held at Chalfonte–Haddon Hall, Atlantic City, May 2-3. The program will consist of three general sessions, a portion of one of which will be set aside for Prof. P. K. Anokin, chief, department of neurophysiology, Academy of the Medical Sciences, U. S. S. R. His subject will be "On the Specific Character of the Activating Influence of the Reticular Formation on the Cerebral Cortex." A fourth session will be allotted to the panel presentation of "Problems of Specificity in Psychosomatic Disorders." This panel will deal with the report of the findings of the long-term study of the Chicago Institute for Psychoanalysis. The registration fee for nonmembers is $5. Students, interns, residents, and fellows will be admitted to the sessions upon payment of $1 and presentation of proper identification. For information, write the American Psychosomatic Society, 265 Nassau Road, Roosevelt, N. Y.

Current Poliomyelitis Morbidity Trends.—The Communicable Disease Center, Atlanta, Ga., reported that during the week ending March 28, there were 19 cases of poliomyelitis reported to the National Office of Vital Statistics, of which 15 were paralytic. The total for the preceding 6-week period was 136 cases, higher than the 84 cases during the comparable period in 1958, but lower than the 215 cases reported during this same interval in 1957. The only known concentration of cases in 1959 has been in Pike County, Mo. Since the last week in December, 15 cases of poliomyelitis were reported from Pike County, by Dr. Edgar A. Belden, director, Bureau of Communicable Disease Control, Missouri Division of Health. All cases were members of an Amish Mennonite Community of about 350 persons divided among 50 families. Of these 15 cases, 7 were paralytic and 8 nonparalytic. One fatality has been reported. The 34 cases reported from Florida, 22 paralytic, are distributed throughout the state, in a pattern following the population density.

Cardiology Meeting in Philadelphia.—The American College of Cardiology will hold its eighth annual convention at the Benjamin Franklin Hotel, Philadelphia, May 25-29, 1959. The program covers recent trends in medical and surgical progress in cardiology. Dr. John S. LaDue, New York City, is national chairman, program committee; Dr. Robert P. Glover, Philadelphia, is advisory chairman to the local committee in charge of convention arrangements; Dr. Seymour Fiske, New York City, is national chairman. Dr. Claude S. Beck, Cleveland, is moderator of a scientific session on surgical problems in coronary and valvular heart disease, featuring new techniques, use and abuse of pump oxygenators, pacemakers, and the evaluation of postoperative syndromes. Dr. Ashton Graybiel, Pensacola, Fla., has arranged a special session on the newer challenges in aviation medicine and the newer aspects of space cardiology. There will be scientific sessions devoted to phonocardiography, ballistocardiography, metabolism, and therapy. Fireside conferences will allow audience participation in discussion of clinical and research problems. For information write the Secretary, Dr. Philip Reichert, American College of Cardiology, Empire State Bldg., New York 1.

Northern Tri-State Meeting.—The 86th annual meeting of the Northern Tri-State Medical Association will be held at the Schuler Hotel, Marshall, Mich., May 7, under the presidency of Dr. James E. Bailey, Coldwater, Mich. The following papers are scheduled:

Open Reduction, Primary and Secondary Fusions in Fractures of the Os Calcis, Dr. Homer H. Stryker, Kalamazoo, Mich., and Dr. Harold J. Meier, Coldwater, Mich.
Diagnosis and Treatment of Peripheral Vascular Disease of the Lower Extremities, Dr. D. Emerick Szilagyi, Detroit.
Investigation and Treatment of Recurrent Urinary Calculus Disease, Dr. William C. Baum, Grand Rapids, Mich.
Commercial Insurance Looks at Blue Cross, R. L. Paddock, president, Time Insurance Company, Milwaukee, Wis.
Laboratory Aids in the Differential Diagnosis of Functional Gynecological Disorders, Gardner M. Riley, Ph.D., Ann Arbor, Mich.
Chemotherapy of Leukemia and Lymphoma, Dr. Frank H. Bethell, Ann Arbor, Mich.

At the luncheon meeting an address will be given by Rev. Calvin Didier, LaPorte, Ind., on "How Much Does The Spirit Weigh." A ladies' program is arranged. For information write Dr. Francis E. Elliott, Northern Tri-State Medical Association, 130 N. Fulton St., Wauseon, Ohio, Secretary-Treasurer.

Bacteriologists Meet in St. Louis.—The 59th general meeting of the Society of American Bacteriologists will be held May 10-14 at the Sheraton–Jefferson and Statler Hotels, St. Louis, with the Eastern Missouri Bacteriologists as hosts. P. R. Edwards, Communicable Disease Center, Chamblee, Ga., president of the society, will open the meeting. The ONR Lecture, "The Three Faces of Immunology," will be given by Ashley A. Miles, of the Lister Institute of Preventive Medicine, London, England. Over 400 papers are scheduled for presentation under four division headings. The following five symposiums are arranged: "Steroid Metabolism," "Biology of Cells Modified by Viruses or Antigens," "Infectious Agents and Phagocytic Cells," "Initiation of Bacterial Growth," and "Microbial Genetics." A. A. Newton, department of pathology, University of Cambridge, England, will give "Infection of Synchronously Dividing HeLa Cells by Herpes Simplex Virus," and "Antimicrobial Properties of Progesterone Analogues" will be given by C. Casas–Campillo, with Dora Balandrano and A. Galarza, Research Laboratories, Syntex, S. A., Mexico, as co-authors. Scientific motion pictures and commercial and scientific exhibits are planned. A program of ladies' activities and tours are arranged. For information write Mr. Samuel G. MacFarlane, 428 E. Preston St., Baltimore 2, Business Manager.

Mental Health Study in South.—A state-by-state study of mental health research in the Southern region has been launched by the mental health program of the Southern Regional Education Board, according to Dr. William P. Hurder, director of the program. The study is designed to get detailed information about the Southern region's resources and needs in mental health and behavioral science research, including research in mental retardation. It will provide an estimate of research projects in progress and how they are being carried out. Over 2,000 questionnaires have been distributed to research personnel and their administrators throughout the region with the cooperation of a committee of research survey chairmen appointed by the governor of each participating state. The cooperation of the Bio-Sciences Information Exchange and the Council of State Governments will supplement the study findings and broaden the scope of the data gathered. The regional mental health program was established in 1954 by the SREB at the request of the Southern Governors' Conference and is supported by an appropriation of $8,000 from each participating state. Its purpose is to aid states and Southern colleges and universities to train more qualified personnel for mental health programs and to aid in securing added support for needed research programs.

Establish Medical Council for Kansas City.—The Medical Council of the Metropolitan Area of Greater Kansas City was formally established at an organizational meeting March 16 in Kansas City. The members are the Clay County (Mo.) Medical Society, Jackson County (Mo.) Medical Society, Johnson County (Kan.) Medical Society, and Wyandotte County (Kan.) Medical Society. The immediate past-president, the president, and the president-elect or vice-president are designated as representatives of the society. The secretaries also attend meetings of the representatives in an ex officio capacity. The Medical Council, following a pattern established in the Washington, D. C. Metropolitan Area and also by the First District Branch of the Medical Society of the State of New York, has the purpose "to unify and give effect to the policies and purposes of the organized medical profession of Greater Kansas City to serve, sustain and promote the public health and welfare in matters involving the Metropolitan Area of Greater Kansas City; to promote programs designed to enhance the health and welfare of the people; and to fulfill on an area level, the established common purposes of the several county medical societies of this Council with due regard to the autonomy and authority of each county medical society." Membership is open to the county medical societies in the Metropolitan Area that may desire to participate. Dr. Dillard M. Eubank, of Kansas City, Mo., was selected chairman.

Establish Fellowship for Physician from India.—The creation of the Merck Sharp & Dohme International Fellowship in Rehabilitation for a physi-

cian from India to undertake advanced training in the United States has been announced. The fellowship will provide a minimum of one year of training in physical medicine and rehabilitation. Initial screening of applications will be done by a committee of Indian leaders in health and medical education. The international fellowship was made possible by a contribution of $10,000 to the World Rehabilitation Fund by the Merck Company Foundation on the recommendation of Merck Sharp & Dohme International Division, Merck & Co., Inc. The fellowship will be administered by the World Rehabilitation Fund, an American voluntary organization, in cooperation with the International Society for the Welfare of Cripples. The latter's affiliate in India is the Indian Society for the Rehabilitation of Crippled Children, of which Dr. Mrs. Gulbanoo Premji, Haji Ali Park, Clerk Road, Mahaluxmi, Bombay, is the national secretary. The World Rehabilitation Fund is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped. Currently there are 71 trainees (57 physicians and 14 nonphysicians) from 35 different nations who receive long-term advanced training in the United States under the auspices of the fund. Its honorary chairmen include Mr. Herbert Hoover, Mr. Harry S. Truman, and Mr. Bernard M. Baruch.

Tornadoes Take Fewer Lives.—The Statistical Bulletin of the Metropolitan Life Insurance Company has stated that the death toll from tornadoes in the United States was lower in the past five years than in any comparable period since the Weather Bureau began to keep systematic records of such storms more than 40 years ago. In the period 1954-1958 tornadoes took about 500 lives, half the loss sustained in each of the preceding five-year periods and little more than one-fourth the toll in 1924-1928. The reduced death toll in recent years reportedly has been due in part to improved tornado detection and warning services. The recent decrease in fatalities has been especially marked in the Southwest. There were 117 tornado deaths in the West South Central region during 1954-1958, compared with 444 five years earlier and with 507 in 1944-1948. Arkansas had only seven tornado deaths in the past five years, a small fraction of the losses suffered in the periods immediately preceding. Texas likewise experienced unusually small numbers of fatalities in recent years. Only three states—all of them in the Midwest—recorded an increasing number of tornado deaths in the period under review. Kansas, which had only five fatalities in 1944-1948 and 11 in the next five years, had 106 deaths in 1954-1958, a greater loss than that experienced by any other state in this period. Wisconsin suffered 37 fatalities in the recent five-year period while Missouri recorded 59 such deaths. The tornado which struck St. Louis early in February of the current year took 21 lives.

Foreign Speakers at Section Centennials.—Seven sections of the Scientific Assembly of the American Medical Association are celebrating their centennials in Atlantic City. Among the centennial participants will be several foreign speakers. R. R. A. Coombs, Ph.D., professor of pathology, University of Cambridge, England, will be the guest centennial speaker for the Section on Pathology and Physiology June 11, in the ballroom of the Shelburne Hotel. His subject will be: "Demonstration of Antigens on Tissue Cells by the Mixed Agglutination Reactions." Mr. Andrew M. Claye, president, Royal College of Obstetricians and Gynecologists, Leeds, England, will be the speaker at a commemorative luncheon in celebration of the 100th anniversary of the founding of the Section on Obstetrics and Gynecology, June 10, in the ballroom of the Sheraton–Ritz Hotel. On June 12, Dr. Coombs and Mr. Claye will be participants in a panel discussion on erythroblastosis fetalis in a joint meeting of the Section on Obstetrics and Gynecology and the Section on Pathology and Physiology, commemorating the 100th anniversary of both sections. This will take place in Trimble Hall, Claridge Hotel. Dr. Jeremy N. Morris, London Hospital Research Laboratories, Ashfield Street, London, will be the guest centennial speaker at the joint meeting of the Section on Experimental Medicine and Therapeutics and the Section on Internal Medicine, which is scheduled for Thursday afternoon in the ballroom of Cenvention Hall. He will take part in a symposium on "Basic Problems of Coronary Disease Today" and will speak on "Occupation and Heart Disease."

Study of Hospital Admissions.—The National Opinion Research Center of the University of Chicago has embarked on a two and one-half year study of hospital admissions. The Health Information Foundation granted $200,000 to the center to investigate the full range of reasons for admitting patients. Chauncy D. Harris, Dean of the Division of Social Sciences of the university and a trustee of the center, announced the grant and said that a systematic study would be made on the medical, social, personal, and professional reasons behind a stay in the hospital. "The aim of this investigation is to develop a better understanding of the role of the hospital and the demands upon it by the community." Of special interest and study will be the bearing of hospital insurance coverage on decisions to hospitalize or not to hospitalize when other factors affecting the decision are controlled, Harris said. Mr. Clyde W. Hart, director of the National Opinion Research Center, said that hospital admissions throughout the nation exceed 20 million annually. He said that

the study for the Health Information Foundation will be based on a sample of admissions to hospitals in the state of Massachusetts. Cooperating will be the Massachusetts Medical Society, the Massachusetts Hospital Association and the Blue Cross–Blue Shield plans in the state. The Health Information Foundation was organized in 1950 as a contribution by the drug, pharmaceutical, chemical, and allied industries to research and education in the social and economic aspects of medical care. The National Opinion Research Center is a specialized research agency affiliated with the University of Chicago. It undertakes specific projects in gaining information on social and scientific problems and collects original data for its reports.

Conference on Legal Environment of Medical Science.—The National Society for Medical Research in conjunction with the University of Chicago has called the first National Conference on the Legal Environment of Medical Science, "to bring order into . . . the laws and regulations governing medical research." The meeting will be held May 27-28 on the University of Chicago campus. Practical problems such as access to cadavers and obtaining animals for humane use in laboratories has stimulated the society, whose membership includes all the accredited medical schools and most medical research associations, to issue a call for clarification of standards. Participants will include scientists, legal scholars, religious leaders, and representatives of various groups affected by differing practice, decisions, and laws. The conference will focus on three major fields: medical experiments on human subjects; medical studies involving the use of dead human bodies; and medical experiments on animal subjects. The conference will attempt to reach agreements on ethical standards for the experimental use of human volunteers, cadavers, and laboratory animals. The conferees will seek to develop principles for a model legal code to govern research in medicine. Rev. Thomas J. O'Donnell, S. J., regent, Georgetown University School of Medicine, will be chairman of the section on human experimentation. Russell T. Woodburne, Ph.D., professor of anatomy, University of Michigan School of Medicine, Ann Arbor, will be the chairman of the section on the use of cadavers. William T. S. Thorp, D.V.M., dean, College of Veterinary Medicine, University of Minnesota, Minnepolis, will be the chairman of the section on animal experimentation. Irvin Ladimer will serve as conference secretary. Inquiries should be addressed to the National Society for Medical Research, 920 S. Michigan Ave., Chicago 5.

Wanted by the FBI.—William Milton Hoffman, who may seek treatment for a stomach ailment and is known to have had tuberculosis, is being sought by the FBI for unlawful flight to avoid confinement for armed robbery. On Feb. 11, 1949, Hoffman was apprehended at Surfside, Fla., and was returned to Michigan, where he was sentenced to serve 10 to 20 years in the State Prison at Jackson. He escaped confinement Oct. 11, 1952. Hoffman has been convicted for burglary, larceny, and armed robbery. He should be considered dangerous. A federal complaint was filed at Detroit in 1956, charging Hoffman with violation of the unlawful Flight to Avoid Confinement Statute. He was born in 1895 in Carter County, Ky.; height 5 ft. 8 in.; weight 128 lbs.; gray hair; blue eyes; medium complexion; race, white; occupation, plumber, telegraph operator. He has ¾-in. scar on back of head; cut scar in left eyebrow; moles below left eye; above right eye; and on right side of chin; ⅝ in. oblique scar below left wrist; two scars on second joint of left thumb; 1 in. oblique scar on palm of right hand near wrist. Hoffman is said to be a gambler, particularly on horse races. He has used these aliases: William

William Milton Hoffman

Halliday; William Jennings Hoffman; Edward Holliday; William Huffman; William Marvin; William Murry; Raymond O'Brien; John Russell; Frank Webber; Frank Williams, and others. Anyone able to assist in locating this fugitive is requested to notify the Director of the Federal Bureau of Investigation, U. S. Department of Justice, Washington 25, D. C., or the Special Agent in Charge of the nearest FBI Division, the telephone number of which may be found on the first page of local telephone directories.

Award in Laryngology and Rhinology.—The American Laryngological Association announced that a sufficient fund has accrued from the Casselberry Fund "for encouraging advancement in the art and science of laryngology and rhinology," and that this sum is now available in part or as a whole, for a prize award. Theses must be in the hands of the Secretary of the American Laryngological Association, Dr. James H. Maxwell, Out-Patient Building, University Hospital, Ann Arbor, Mich., by Jan. 1. The Casselberry Award is a prize of money with

accompanying certificate. The sum of money will be agreed upon by the council of the association after the manuscript has been evaluated by the Award Committee. It may be awarded in whole or in part among several contestants. Eligible contestants may be: (1) hospital interns, residents, or graduate students in rhinology and laryngology; (2) an individual with an M.D. degree actively practicing or teaching rhinology and laryngology in the Americas; (3) any scientific worker in rhinology and laryngology. Manuscripts shall be presented under nom de plume which shall in no way indicate the author's identity. There shall also be a sealed envelope bearing the nom de plume and containing a card showing the name and address of the contestant which the secretary shall keep. Manuscripts must be limited to 5,000 words and must be typewritten, double spaced on one side of the sheet. The thesis shall not have been published elsewhere. The successful thesis shall become the property of the association but this provision shall in no way interfere with publication of the thesis in the journal of the author's choice. Unsuccessful contributions will be returned promptly. The award, to be made at the annual meeting of the American Laryngological Association, shall be based on: originality of material; scientific and clinical value; suitability for this award; method of presentation as to style, illustrations, and references. The maximum amount shall not exceed $200.

FOREIGN

Plan Rehabilitation Center in Philippines.—What is reportedly the first community rehabilitation center in the Far East is to be developed in San Pablo, the Philippines, the Republic of the Philippines Ambassador to the United States, Carlos P. Romulo, announced in a press conference held at the Institute of Physical Medicine and Rehabilitation, New York City. Also participating in the press conference were Mr. George Hampton, senior executive vice-president, whose company, General Foods Corporation, granted the funds for the project, and Dr. Howard A. Rusk, president, World Rehabilitation Fund, and director, Institute of Physical Medicine and Rehabilitation. The San Pablo Rehabilitation Center is an out-patient rehabilitation center. It will provide medical, physical therapy, social work, prosthetics, bracemaking, and related rehabilitation services to the community of San Pablo. In addition to a medical director, the center will have a full-time staff of nine persons initially. Dr. Rusk explained that although there are a number of governmental or university-operated rehabilitation centers in the Far East including that of the National Orthopedic Hospital in Manila, the San Pablo Rehabilitation Center is the first to be community-sponsored and community-operated. Six physicians from the Philippines have returned to the Philippines within the past three years after receiving long-term postgraduate training in physical medicine and rehabilitation within the Department of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, and six additional physicians and a social worker from the Philippines are currently enrolled in such advanced training.

CORRECTIONS

Committee on Hypnosis.—The item in the Organization Section entitled "New Committee on Hypnosis" (March 21, page 1339) inadvertently omitted the fact that Dr. M. Ralph Kaufman of New York a member of the Council on Mental Health of the American Medical Association was appointed by the Chairman of the Council, Dr. Leo H. Bartemeier, as liaison member to the Council's new Committee.

Unlawful Practice.—The foreign letter from Canada entitled "Unlawful Practice Charge" (March 14 issue of THE JOURNAL, page 1225) states "For this purpose it was not required that he be licensed in the province (a step which would have involved an internship and examination)." This clause in parentheses is not true. An English physician who has been engaged by the Canadian Department of Indian Affairs to treat Indians, being a graduate of a British university and having his name on the General Register of the General Medical Council of the United Kingdom, would not have to do further internship before he could be licensed in this province. He simply has to furnish the College of Physicians and Surgeons of Ontario with certain information and/or documents, pay a small fee, and then write the Medical Council of Canada examinations.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing application is June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARKANSAS:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Written.* San Francisco, June 15-18; Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* San Francisco, June 13; Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* San Francisco, June 14; Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

DELAWARE: *Examination.* Dover, July 14-16. *Endorsement.* Dover, July 23. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

DISTRICT OF COLUMBIA:* *Written.* Washington, June 8-9. Final date for filing application is May 1. Sec., Dr. Daniel Leo Finucane, 1740 Massachusetts Ave., N. W., Washington.

FLORIDA:* *Examination.* Miami Beach, June 21-23. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, June 10-11. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

HAWAII: *Written.* Honolulu, July 13-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: *Examination and Endorsement.* Boise, July 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

INDIANA: *Examination.* Indianapolis, June 17-19. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

IOWA:* *Examination.* Iowa City, June 15-17. Exec. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines 19.

KANSAS:* *Examination and Endorsement.* Kansas City, June. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 8-10. Sec., Dr. Russell E. Teague, 620 South Third St., Louisville 2.

LOUISIANA: *Examination and Reciprocity.* New Orleans, June 4-6. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans.

MARYLAND: *Examination.* Baltimore, June 23-26. Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

MISSISSIPPI: *Examination and Reciprocity.* Jackson, June 22-24. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

MISSOURI: *Examination.* St. Louis, May 29-30. Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Bldg., Jefferson City.

NEBRASKA:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 16-19. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton 8.

NEW MEXICO:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

NEW YORK: *Examination.* New York, Rochester, Syracuse, Buffalo and Albany, June 23-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Written. Examination and Endorsement.* Raleigh, June 15-18. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination and Reciprocity.* Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

OHIO: *Examination.* Columbus, June 18-20. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

PENNSYLVANIA: *Examination and Endorsement.* Philadelphia and Pittsburgh, July 1-3. Sec., Mrs. Margaret G. Steiner, Box 911 Harrisburg.

PUERTO RICO: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

SOUTH CAROLINA: *Reciprocity.* Columbia, May 12; *Examination.* Columbia, June 23-24. Sec., Dr. H. E. Jervey, Jr., 1829 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination and Reciprocity.* Salt Lake City, July 810. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: *Examination.* Richmond, June 18-20. *Endorsement.* Richmond, June 17. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

VIRGIN ISLANDS: *Examination.* Charlotte Amalie, St. Thomas, June 10. Chairman, Dr. Melvin H. Evans, Christiansted, St. Croix.

WASHINGTON:* *Examination.* Seattle, July 13-15. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WEST VIRGINIA: *Examination.* Charleston, June. Sec., Dr. Newman H. Syer, State Office Bldg., No. 3, Charleston 5.

WISCONSIN:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

WYOMING: *Examination and Reciprocity.* Cheyenne, June 1. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

COLORADO: *Examination.* Denver, May 6-7. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

CONNECTICUT: *Examination.* New Haven, June 6. Exec. Asst. Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, May 18-19. Address: Mr. Paul Foley, Deputy Director, 1740 Massachusetts Ave., N. W., Washington.

FLORIDA: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

KANSAS: *Examination.* Kansas City, June 2-3. Sec., Dr. L. C. Heckert, Pittsburg.

MICHIGAN: *Examination.* Ann Arbor and Detroit, May 8-9. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

NEBRASKA: *Examination.* Omaha, May 5-6. Director, Mr. R. K. Kirkman, Bureau of Examining Boards, 1009 State Capitol Bldg., Lincoln.

SOUTH DAKOTA: *Examination.* Vermillion, June 5-6. Sec., Dr. Gregg M. Evans, 310 East 15th St., Yankton.

WASHINGTON: *Examination.* Seattle, July 8-9. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WISCONSIN: *Examination.* Milwaukee, June 6. Madison, Sept. 11. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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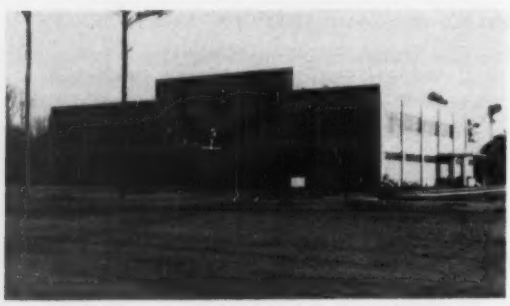
*Basic Science Certificate required.

GOVERNMENT SERVICES

AIR FORCE

Medical Officers Honored.—Col. Herbert W. Coone, U. S. A. F. (MC), was presented the Air Force Commendation Medal for meritorious service as Chief of Professional Services and Deputy Commander of the U. S. A. F. Hospital at Wiesbaden, Germany, from February, 1956, to December, 1958. During this period, the hospital underwent an unprecedented growth in workload and stature as the principal medical and surgical center for the United States Air Force in Europe. Doctor Coone was cited for his leadership and perseverance in improving the medical standards and for his conscientious research of preventive medicine and the community health program which resulted in an unprecedentedly low noneffective rate. Col. Ralph M. Lechausse, U. S. A. F. (MC), was presented the Legion of Merit for his meritorious performance of duty as Surgeon of Joint Task Force 7 during the 1958 nuclear tests in the Pacific. He was cited for his thorough investigation of possible exposure hazards to radiation resulting from nuclear tests and for creating and maintaining excellent international relationships in conducting such investigations.

New U. S. A. F. Hospital.—The new 50-bed U. S. A. F. Hospital at Myrtle Beach Air Force Base, S. C., was opened on March 1. This two-story,



air-conditioned hospital offers outpatient service, including clinics in internal medicine, obstetrics, and surgery. Medical, surgical, and obstetrical facilities for inpatient care are located on the second floor. Col. Paul E. Lance, M. S. C., U. S. A. F., is commander of the hospital.

VETERANS ADMINISTRATION

Dr. Barnwell Honored.—The Veterans Administration's top award, the Exceptional Service award, was presented to Dr. John B. Barnwell, the agency's chief of medical research and education. Dr. Barnwell was cited for his part in organization of the VA-Armed Forces cooperative study of the chemotherapy of tuberculosis and for his leadership as VA assistant chief medical director for research and education. The VA-Armed Forces study, begun under Dr. Barnwell when he was chief of the VA tuberculosis service in 1946 and still continuing under that service, has played a large part in giving medicine modern drug treatments for tuberculosis.

Personal.—Dr. John M. Rumball, chief of medical service at the Veterans Administration hospital in Coral Gables, Fla., was appointed director of medical service for the agency in Washington, D. C., effective early in April. He also has accepted an appointment as clinical associate professor of medicine at Georgetown University School of Medicine in Washington, D. C.

FOOD AND DRUG ADMINISTRATION

Kelp Won't Help Your Diet.—Promoters of worthless products falsely represented as sources of additional vitamins and minerals in the diet and cures for disease continue to cheat the consumer and endanger his health. Each year, such promoters take from the American people large sums of money that could better be spent for wholesome, nutritious foods or competent medical advice. The Food and Drug Administration announced the seizure of 23,000 tablets of a so-called dietary supplement made with alfalfa, kelp, and brewer's yeast. The promoter claimed the tablets contained significant amounts of 14 vitamins, 10 minerals, and 14 proteins. His label carried an impressive-looking list of the amounts as measured in U. S. P. units. Agency analysts found the tablets did not contain amounts of vitamins, minerals, or proteins that could be measured in U. S. P. units. Kelp, one of the ingredients, is a source of iodine, which is already supplied in the diet. Alfalfa is a livestock feed. Brewer's yeast is used to make beer. Such ingredients do not prevent illness or generate health as claimed.

Pure Food Violations.—Tomato products and bulk wheat and rice continued to make up the largest volume of unfit foods removed from the market in February; 40 shipments totaling 886 tons of contaminated foods were seized. Of this amount, 293 tons of canned tomatoes in a single shipment were contaminated with fly eggs and maggots. More than 38 tons of other tomato products, including paste, puree, pizza sauce, catsup, and soup, contained spoiled tomatoes or fly eggs and maggots.

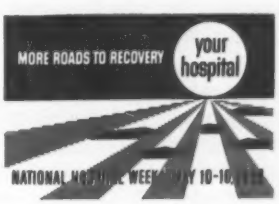
Two hundred ninety-six tons of wheat and rice were contaminated with rodent pellets, urine, hairs, and insect parts; 166 of the 179 tons of unfit warehoused foods was in rodent-contaminated chick peas (140 tons) and moldy, wormy, insect-damaged green coffee beans (26 tons) seized together in a New York warehouse.

An additional 58 tons of foods and 20,100 vitamin capsules were seized because of hazards to health. Included were 52 tons of mercury-contaminated wheat and 6 tons of an oil feed ingredient in which mineral oil had been substituted for edible oil. The vitamin product was deficient in vitamin B_1. Another 7 tons of foods seized as economic cheats included an instant chocolate flavored mix that was misbranded by false and misleading claims, an olive oil product in which teaseed oil was substituted for olive oil, and black pepper in which ground buckwheat hulls were substituted for black pepper. Of 10 drugs and devices seized in February, 3 were alleged to be misbranded by false and misleading claims. A medicated chest plaster was sold directly to parents as a four-day treatment for children's whooping cough, croup, spasmodic asthma, and hoarseness due to colds. Capsules of two prescription drugs—an amphetamine and a barbiturate—were substandard in rate of disintegration and drug content.

Truckdrivers Sentenced in Rotten Egg Racket.—Activities of the rotten egg combine continued in February despite numerous seizures and the threat of prison sentences hanging over key operators who are on probation. Egg shipments valued at $15,000 were seized at Eastern Seaboard cities from New York to Florida. On June 6 and 7, 1957, Food and Drug inspectors and state police followed a truckload of rotten eggs from central Maine, across New Hampshire, Massachusetts, and New York, and into New Jersey. For identification the inspectors had marked the eggs with an invisible crayon, which can only be seen under ultraviolet light. The driver reached speeds of 90 to 100 miles an hour during the 500-mile pursuit. Reaching Newark, N. J., ahead of his pursuers, he abandoned the truck and its cargo in a parking lot. Inspectors and U. S. Deputy Marshals maintained surveillance over the truck for five days before the marshal was able to serve seizure papers. The driver pleaded guilty to charges of interstate transportation of these eggs on Oct. 7, 1958. A day or two later he was reported to have made another pickup of rotten eggs at New England hatcheries. A week later he was apprehended in Vermont with a load of rotten eggs. At his sentencing, the court pointedly asked him if his family still ate eggs. On Feb. 13, 1959, the federal court at Newark, N. J., fined him $500 and placed him on probation for five years.

Pharmacists Convicted for Unauthorized Drug Refills.—A pharmacist-owner in Livingston, N. J., and a pharmacist-employee were convicted for unauthorized refilling of prescriptions for barbiturates and amphetamine. They dispensed up to four refills on the same prescription, voluntarily offering to double and triple the physician's recommended dosage and furnishing the increased amounts in subsequent refills. In one instance, a bottle of 100 capsules was sold as a refill of a prescription calling for only 12. The amount of money saved by purchasing drugs in large quantities was pointed out to Food and Drug inspectors, posing as customers. Federal Judge Thomas F. Meany (Newark, N. J.) said the temptation for extra profit in this case created a dangerous situation which could have fatal consequences. The court fined the owner a total of $3,000 on four counts and the employee $300 on one count.

Voluntary Corrective Actions.—Food manufacturers and warehousemen voluntarily spent a total of $96,985 during February in plant improvements suggested by agency inspectors to assure production of clean, wholesome products. A Pennsylvania baker eliminated possible insect contamination of his product at a cost of $35,000. He revamped his equipment for easy cleaning, stepped up his schedule of spraying for insects, and arranged to get regular advice on sanitation problems. A California olive oil producer spent $11,590 to correct insanitary practices in handling olives. A steam boiler, hopper, shaker screen and washing set-up, stainless steel holding tank, and special filter were among new items of equipment that he installed to process his raw materials more rapidly and keep them clean and unspoiled. Food firms voluntarily destroyed or converted to nonfood use more than 973 tons of unfit foods. Drug plants and warehouses voluntarily destroyed old and substandard drugs valued at $47,826.



DEATHS

Albright, George Carter Ⓜ Iowa City, Iowa; born in Pleasant Grove, Iowa in 1881; State University of Iowa College of Medicine, Iowa City, 1914; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served as vice-president of the Iowa State Medical Society; for 10 years president of the Johnson County Tuberculosis Association; in 1956 recipient of a medallion awarded by the Iowa Tuberculosis Association for his long and outstanding service to the group; past-president of the board of education; associated with the Mercy Hospital and the University Hospital, where he died Feb. 1, aged 77.

Alling, Marshall Louis Ⓜ Lowell, Mass.; Dartmouth Medical School, Hanover, N. H., 1909; fellow of the American College of Surgeons; veteran of World War I; served as medical examiner for the Middlesex North District; associated with St. Joseph's and Lowell General hospitals, and St. John's Hospital, where he died Feb. 8, aged 74.

Alspach, Walter Louis Ⓜ Miami, Fla.; University of Buffalo School of Medicine, 1918; associated with Mercy and Jackson Memorial hospitals; died Feb. 11, aged 64.

Ames, Sheppard Kellam Ⓜ Cape Charles, Va.; University of Virginia Department of Medicine, Charlottesville, 1925; interned at St. Joseph's Hospital in Baltimore; served overseas during World War I; member of the staff and board of trustees of the Northampton–Accomack Memorial Hospital in Nassawadox; died Jan. 30, aged 63.

Ausbrooks, Munch Trousdale, Smartt, Tenn.; University of Tennessee Medical Department, Nashville, 1895; postmaster; died in McMinnville Jan. 30, aged 88.

Baer, Raymond Bernhard Ⓜ Detroit; University of Chicago, The School of Medicine, 1931; specialist certified by the American Board of Obstetrics and Gynecology; veteran of World War I; clinical instructor in obstetrics and gynecology at Wayne University College of Medicine; associated with Receiving Hospital, St. Mary's Hospital, and Jennings Memorial Hospital, where he died Feb. 7, aged 59.

Barone, Samuel Ⓜ Buffalo, N. Y.; University of Buffalo School of Medicine, 1916; veteran of World War I; member of the American Academy of General Practice; on the staffs of the Deaconess and Lafayette General hospitals; died in the Millard Fillmore Hospital Jan. 29, aged 68.

Blount, Dillon Jefferson Jr. Ⓜ Mandeville, La.; University of Arkansas School of Medicine, Little Rock, 1946; member of the American Psychiatric Association; interned at the Charity Hospital of Louisiana in New Orleans; served a residency at the Veterans Administration Hospital in New Orleans; from 1946 to 1949 an officer in the medical reserve corps of the U. S. Army; formerly on the staff of the East Louisiana Hospital in Jackson; served on the staff of the Veterans Administration Hospital in Murfreesboro, Tenn.; superintendent of the Southeast Louisiana Hospital; died Jan. 28, aged 36.

Bolduc, Valmore Elmer, Nashua, N. H.; University of Vermont College of Medicine, Burlington, 1921; veteran of World War I; served as school physician; formerly city physician; on the staffs of St. Joseph's and Nashua Memorial hospitals; died Jan. 31, aged 61.

Bonar, Ethel Casto, Chicago; Western Reserve University School of Medicine, Cleveland, 1927; died Nov. 26, aged 65.

Boone, James Lunsford Ⓜ Green Cove Springs, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1917; specialist certified by the American Board of Otolaryngology; past-president of the Duval County Medical Association; veteran of World War I; on the staffs of the Baptist Memorial, St. Vincent's, St. Luke's, and Riverside hospitals in Jacksonville; died in Jacksonville Feb. 14, aged 64.

Bowers, James Michael Ⓜ Seattle; University of Michigan Medical School, Ann Arbor, 1925; fellow of the American College of Physicians; clinical assistant professor of medicine at the University of Washington School of Medicine; past-president of the Seattle Academy of Internal Medicine; veteran of World War II; on the staff of the Providence Hospital; died Feb. 9, aged 58.

Brackney, Edwin Leland Ⓜ Windermere, Fla.; the Hahnemann Medical College and Hospital, Chicago, 1915; served as a fellow in surgery and an instructor in surgery at the University of Minnesota Medical School in Minneapolis; later named assistant professor of surgery at the Medical College of Georgia in Augusta; served with the medical corps of the U. S. Army from 1947 to 1949 and from 1950 to 1952; died in Orlando Nov. 13, aged 70.

Ⓜ Indicates Member of the American Medical Association.

Browning, Lawrence T., Peach Creek, W. Va.; University of Louisville (Ky.) School of Medicine, 1926; died Feb. 3, aged 55.

Buckner, Doster Ⓜ Fort Wayne, Ind.; Indiana University School of Medicine, Indianapolis, 1919; member of the American Academy of General Practice; associated with Lutheran and Parkview Memorial hospitals; died Feb. 2, aged 66.

Bukowski, Edward Branislaus Ⓜ Buffalo, N. Y.; born in Buffalo Sept. 29, 1898; University of Buffalo School of Medicine, 1923; specialist certified by the American Board of Preventive Medicine; assistant professor of preventive medicine and public health, University of Buffalo School of Medicine; instructor of public health administration, Syracuse University, from 1941 to 1943; appointed health commissioner of the City of Buffalo in 1947 and in that position helped lay the groundwork for organization of the present Erie County Health Department which took over the city health department in 1948; appointed first deputy commissioner of the Erie County Health Department and held that office until appointed commissioner in April, 1955; died Feb. 21, aged 60.

Burghardt, Michael Ⓜ Brooklyn; Long Island College of Medicine, Brooklyn, 1931; fellow of the American College of Surgeons; veteran of World War II; associated with the Luther Medical Center, Norwegian Hospital, and Prospect Heights Hospital; died Jan. 10, aged 54.

Candela, Rolando Diaz Ⓜ Chicago; Universidad de la Habana Facultad de Medicina y Farmacia, Cuba, 1943; an officer in the medical reserve corps of the U. S. Army from Feb. 12, 1953 to April 30, 1956, interned at the Unity Hospital in Brooklyn; served a residency at the Adelphi Hospital, Brooklyn Women's Hospital, Prospect Heights Hospital, and the Caledonian Hospital, all in Brooklyn; died in the West Side Veterans Hospital Nov. 8, aged 39.

Carlisle, Patrick G., Connersville, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1904; past-president of the Fayette County Board of Health; died in the Fayette Memorial Hospital Dec. 27, aged 80.

Carpenter, Robert Morse Ⓜ Stamford, Conn.; Chicago College of Medicine and Surgery, 1916; veteran of World War I; past-president of the Stamford Medical Society; president of the medical staff at Stamford Hospital and attending physician at St. Joseph's Hospital, where he died Feb. 7, aged 64.

Carpenter, William McNeill Ⓜ Greenville, S. C.; Johns Hopkins University School of Medicine, Baltimore, 1927; certified by the National Board of Medical Examiners; died Feb. 7, aged 56.

Cassidy, William J. Ⓜ Detroit; Detroit College of Medicine, 1908; also a pharmacist; past-president of the Wayne County Medical Society and of the Detroit Academy of Surgery; veteran of World War I; member of the Radiological Society of North America; fellow of the International College of Surgeons; served on the faculty of his alma mater; at various times associated with St. Mary's, Children's, Providence, Mount Carmel, Brent General, Holy Cross, and Delray General hospitals; staff physician for the *Detroit News;* died Feb. 11, aged 78.

Charbonnet, Louis Sr. Ⓜ New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1901; for many years on the staff of the Hotel Dieu; died Feb. 3, aged 80.

Cheney, William Whittlesey, Fall City, Wash.; University of Michigan Homeopathic Medical School, Ann Arbor, 1892; also a pharmacist; served on the staff of the Nelems Memorial Hospital in Snoqualmie; died in Redmond Feb. 15, aged 91.

Cherwin, Nathan Hale Ⓜ Los Angeles; Columbia University College of Physicians and Surgeons, New York City, 1924; veteran of World War I; died in Las Vegas, Nev., Dec. 21, aged 59.

Christmann, Paul, Glendale, Calif.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1903; veteran of World War I; served on the staffs of the Behrens Memorial and Glendale hospitals; died in the Veterans Administration Hospital in Los Angeles Dec. 25, aged 79.

Clark, James Walker Ⓜ Durango, Colo.; University of Texas School of Medicine, Galveston, 1941; member of the American Academy of General Practice; served in the medical corps of the U. S. Naval Reserve during World War II; on the staff of the Mercy Hospital; died Feb. 4, aged 43.

Clark, William Henry G., St. Louis; Meharry Medical College, Nashville, Tenn., 1912; died in St. Mary's Infirmary Jan. 20, aged 84.

Cleveland, Frank Mortimer Ⓜ Philadelphia; Jefferson Medical College of Philadelphia, 1899; veteran of World War I; at one time on the faculty of Woman's Medical College of Pennsylvania; on the staff of the Presbyterian Hospital; died in Ambler, Pa., Jan. 29, aged 87.

Colantuono, Julius George Ⓜ Locust Valley, N. Y.; Albany (N. Y.) Medical College, 1946; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War II; lieutenant commander in the medical corps of the U. S. Naval Reserve from 1954 to 1956; on the staffs of the

Community Hospital in Glen Cove, Hillside Hospital, Glen Oaks, and Queen's General Hospital in Jamaica; died Feb. 4, aged 37.

Cooper, William Morris Ⓜ New York City; New York Homeopathic Medical College and Flower Hospital, New York City, 1921; fellow of the American College of Surgeons; formerly adjunct professor of surgery at New York Polyclinic Medical School and Hospital; served on the staffs of the Midtown and St. Clare's hospitals; died Feb. 16, aged 64.

Cornell, Howard Merritt, Albuquerque, N. M.; Kansas City (Mo.) Medical College, 1892; formerly associated with the Indian Service; died in St. Margaret's Hospital, Montgomery, Ala., Feb. 2, aged 88.

Crowe, John Alexander Ⓜ San Francisco; Creighton University School of Medicine, Omaha, 1931; interned at Southern Pacific General Hospital; associated with St. Mary's Hospital, where he died Dec. 20, aged 54.

Curl, Robert Bruce, Toledo, Ohio; Eclectic Medical College, Cincinnati, 1916; served overseas during World War I; formerly associated with the city board of health and the board of education; on the staffs of the Flower and St. Luke's hospitals; died in the Veterans Administration Hospital, Dearborn, Mich., Jan. 29, aged 81.

Darche, Albert A. Ⓜ Westbrook, Maine; Laval University Faculty of Medicine, Quebec, Que., Canada, 1919; served with the Canadian Army during World War I; died in Portland Jan. 13, aged 63.

Davis, Frederick Upham, Fairbault, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; served as health officer of Faribault; veteran of the Spanish–American War; for many years served as the head of the Rice County Selective Service Board; a charter member of the Faribault Chapter of Rotary International and served as the second president of that organization; area council president of the Boy Scouts of America, and was the recipient of the Silver Beaver Award for distinguished service to boyhood; on the staff of St. Lucas Deaconess Hospital; died Jan. 23, aged 83.

De Motte, Roy James Ⓜ Chicago; Rush Medical College, Chicago, 1912; fellow of the American College of Surgeons; on the staff of the Roseland Community Hospital; for many years chief surgeon for the Pullman Standard Car Manufacturing Company; died Feb. 16, aged 77.

Dolan, Martin Aloysius Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1932; associated with the Little Company of Mary, St. George, and Cook County hospitals; died Feb. 19, aged 51.

Eckert, M. Milton Ⓜ New York City; Long Island College Hospital, Brooklyn, 1911; member of the Association of Military Surgeons of the United States; veteran of World War I; died Jan. 11, aged 70.

Eichert, Herbert Ⓜ Miami, Fla.; born in Baltimore May 28, 1907; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1932; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member and past-vice-president of the American College of Cardiology; past-vice-president of the Florida Heart Association; past-president of the Miami Heart Association; clinical associate professor of internal medicine at the University of Miami School of Medicine in Coral Gables, where he was past-secretary of the medical board; veteran of World War II; past-director of cardiology at Jackson Memorial Hospital and chief of staff of the National Children's Cardiac Home; chief of medicine at Mercy Hospital; since 1949 consultant in cardiology at the Veterans Administration; died Feb. 2, aged 51.

Fagin, Joseph Ⓜ Long Beach, Calif.; Long Island College of Medicine, Brooklyn, 1938; interned at the Greenpoint Hospital in Brooklyn; served a residency in obstetrics and gynecology at Henry Ford Hospital in Detroit; specialist certified by the American Board of Obstetrics and Gynecology; member of The Endocrine Society; director of medical research at Ciba Pharmaceutical Company during 1940-1944; associated with St. Mary's Community, and Seaside Memorial hospitals; died Dec. 9, aged 55.

Faragher, James Lawrence Ⓜ Cleveland; Western Reserve University School of Medicine, Cleveland, 1913; fellow of the American College of Surgeons; associated with Marymount Hospital in Garfield Heights, St. Vincent Charity Hospital and St. Alexis Hospital, where he died Feb. 6, aged 69.

Fellows, Walter Lesley, Philadelphia; Hahnemann Medical College of Philadelphia, 1904; died Jan. 14, aged 80.

Franklin, Wellington August, Kinmundy, Ill.; John A. Creighton Medical College, Omaha, 1896; died in Manhattan Beach, Calif., Jan. 1, aged 85.

Galloway, Quince Rudolph Ⓜ Livermore, Calif.; University of Nashville (Tenn.) Medical Department, 1906; died Jan. 29, aged 87.

Gardner, Wray Rodgers Ⓜ Denver; University of Colorado School of Medicine, Denver, 1930; member of the American Psychiatric Association; clinical instructor in psychiatry at his alma mater; past-secretary of the Colorado Neuropsychiatric Society; served as director of mental health for the Colorado

State Public Health Department; veteran of World War II; associated with Mount Airy Hospital; on the staffs of General Rose Memorial, St. Luke's, and St. Joseph's hospitals; died Jan. 28, aged 54.

Glenn, Grover Cleveland Ⓜ State College, Pa.; Eclectic Medical College of the City of New York, 1912; veteran of World War I; died in the Bloomsburg (Pa.) Hospital Jan. 25, aged 72.

Lussier, Joseph Hermenegilde, Springfield, Mass.; Boston University School of Medicine, 1922; interned at the Massachusetts Homeopathic Hospital in Boston; fellow of the American College of Surgeons; veteran of World War I; for many years on the staff of the Mercy Hospital, where he died Jan. 30, aged 61.

McGill, Caroline Ⓜ Gallatin Gateway, Mont.; Johns Hopkins University School of Medicine, Baltimore, 1914; past-president of the Silver Bow County Medical Society; formerly practiced in Butte, where she was on the staff of the Murray Hospital; in October, 1955, was named "Woman of the Year" by the Butte Business and Professional Women's Club; in 1955 awarded an honorary doctor of science degree at Montana State College in Bozeman; died Feb. 4, aged 79.

Miller, James Patton Ⓜ Baltimore; Columbia University College of Physicians and Surgeons, New York City, 1940; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; veteran of World War II; assistant instructor of pathology at the University of Pennsylvania School of Medicine in Philadelphia, 1940-1941; assistant professor of orthopedic surgery at Johns Hopkins University School of Medicine; associated with Johns Hopkins Hospital and James Lawrence Kernan Hospital for Crippled Children; died Feb. 1, aged 45.

Moore, Milton H., Dearborn, Mo.; Ensworth Medical College, St. Joseph, 1896; served three terms as mayor of Dearborn and coroner of Platte County; died in Missouri Methodist Hospital in St. Joseph Jan. 27, aged 87.

Newman, William Manning Ⓜ Spokane, Wash.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; formerly county health officer; honorary staff member of Deaconess, Sacred Heart, and St. Luke's hospitals; died Jan. 11, aged 87.

Patterson, John Norman Ⓜ Burlington, Iowa; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1890; died Jan. 7, aged 94.

Pearson, Fray Owen Ⓜ Macon, Ga.; Vanderbilt University School of Medicine, Nashville, Tenn., 1929; regional director of public health for the state of Georgia; served as director of the Chattanooga–Hamilton County (Tenn.) Health Department; formerly on the staff of the Knoxville, Tenn., health department; died Jan. 9, aged 55.

Pease, Willard A., Rio, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1902; died in Waterloo Jan. 24, aged 82.

Perkins, Robert Donald Ⓜ Moline, Ill.; Rush Medical College, Chicago, 1935; member of the American Urological Association; fellow of the American College of Surgeons; during World War II served overseas in the European Theater for three years; associated with St. Anthony Hospital in Rock Island and the Lutheran Hospital; past-president of the medical staff and chairman of the executive committee of the Moline Public Hospital, where he died Dec. 31, aged 49.

Phillips, Julius Andrew, Minden, La.; Meharry Medical College, Nashville, Tenn., 1927; secretary of the Keystone Life Insurance Company; medical director of the Phillips Hospital, of which he was the owner; died Jan. 12, aged 62.

Pinson, Charles Campbell Ⓜ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1926; fellow of the American College of Surgeons; associated with the Baptist Memorial and the Robert B. Green Memorial hospitals, and the Santa Rosa Hospital, where he died Jan. 1, aged 59.

Projector, Harry Ⓜ Washington, D. C.; University and Bellevue Hospital Medical College, New York City, 1913; for many years practiced in New York City, where he was on the staff of the Bronx Hospital; died Jan. 29, aged 74.

Propst, Duane Willard Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1919; formerly on the faculty of his alma mater; author of "The Patient Is the Unit of Practice"; died in the Presbyterian–St. Luke's Hospital Feb. 2, aged 67.

Rader, John Franklin Ⓜ Houston, Texas; University of Texas School of Medicine, Galveston, 1926; veteran of World War I; co-founder of the Parkview Hospital, where he died Jan. 27, aged 61.

Reis, Abilio Gomez da Silva Ⓜ Piedmont, Calif.; Universidade de Lisboa Faculdade de Medicina, Portugal, 1919; fellow of the International College of Surgeons and the American College of Surgeons; member of the staff of the Peralta Hospital in Oakland; died Feb. 1, aged 66.

Ritenour, Almer Daniel Ⓜ Jamestown, Ohio; University of Cincinnati College of Medicine, 1922; served as president of the Greene County Board of Health; associated with the Greene Memorial Hospital in Xenia, where he died Jan. 24, aged 69.

Rosenberg, Lionel, Brooklyn; Long Island College Hospital, Brooklyn, 1907; specialist certified by the American Board of Internal Medicine; associate clinical professor of medicine at the New York Medical College, Flower and Fifth Avenue Hospitals, New York City; died Feb. 6, aged 75.

Rosenstein, Harry, New York City; Fordham University School of Medicine, New York City, 1917; served overseas during World War I; on the staffs of the Misericordia Hospital and the Lebanon Hospital, where he died Jan. 30, aged 66.

Rossow, Russell Julius Ⓜ Evansville, Ind.; Washington University School of Medicine, St. Louis, 1939; member of the American Academy of General Practice; past-treasurer of the Vanderburgh County Medical Society; past-president of the Baptist Hospital staff; died in the Vanderbilt University Hospital, Nashville, Tenn., Jan. 10, aged 56.

Rowley, Philip William, Dunedin, Fla.; Tufts College Medical School, Boston, 1918; formerly practiced in Gloucester, Mass., where he was on the staff of the Addison Gilbert Hospital; died in the Mease Hospital Jan. 17, aged 65.

Ruoff, Andrew C. Ⓜ Union City, N. J.; Fordham University School of Medicine, New York City, 1917; also a lawyer; taught medical jurisprudence at John Marshall College; on the courtesy staff of the North Hudson Hospital; died in the Doctors Hospital in New York City Jan. 21, aged 65.

Savage, Francis Joseph Ⓜ St. Paul, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1901; past-president of the Minnesota State Medical Association and the Ramsey County Medical Society; from 1940 to 1947 member of the House of Delegates of the American Medical Association; fellow of the American College of Surgeons; veteran of World War I; associated with St. Luke's Hospital; for many years a surgeon for the Great Northern Railway; died Jan. 16, aged 83.

Schilback, Harold Fenwick, New Milford, Conn.; Long Island College of Medicine, Brooklyn, 1932; specialist certified by the American Board of Ophthalmology; formerly practiced in Brooklyn, where he was on the staffs of the Brooklyn Eye and Ear Hospital and Long Island College Hospital; on the staff of the New Milford Hospital; died in New Haven Hospital Jan. 14, aged 58.

Schoonmaker, Guy Daniel Ⓜ San Francisco; Vanderbilt University School of Medicine, Nashville, Tenn., 1917; member of the American Academy of General Practice; died Jan. 14, aged 67.

Schrup, Joseph Henry Ⓜ Dubuque, Iowa; Northwestern University Medical School, Chicago, 1904; veteran of World War I; associated with Finley and St. Joseph Mercy hospitals; died Jan. 10, aged 76.

Seeley, Isaac Flood, Tucson, Ariz.; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1904; died in Tucson Medical Center Jan. 3, aged 77.

Seidelmann, Otto Frank Ⓜ Chicago Heights, Ill.; Chicago Medical School, 1941; veteran of World War II; associated with St. James Hospital, where he died Jan. 29, aged 44.

Sekiyama, Isami Ⓜ Los Angeles; Tohoku Imperial University Medical Faculty, Sendai, Japan, 1915; died Jan. 19, aged 67.

Shearer, Amon Robert Ⓜ Mont Belview, Texas; University of Texas School of Medicine, Galveston, 1898; past-president of the Liberty–Chambers Counties Medical Society; assistant county health officer; died in the Polk County Hospital, Livingston, Jan. 16, aged 87.

Sherard, Stuart Baskin Ⓜ Gaffney, S. C.; University of Maryland School of Medicine, Baltimore, 1905; past-president of the Cherokee County Medical Society; associated with the Cherokee County Memorial Hospital; died Jan. 2, aged 79.

Sherwood, William Davies Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1906; specialist certified by the American Board of Psychiatry and Neurology; served in France during World War I; formerly on the faculty of the New York Post-Graduate Medical School, Columbia University; fellow of the Academy of Compensation Medicine and the New York Society for Clinical Psychiatry; associated with the University and Willard Parker hospitals died Feb. 1, aged 76.

Simons, Harold R., San Francisco, Calif.; Loyola University School of Medicine, Chicago, 1929; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the International College of Surgeons; resigned from the regular Navy in 1931; veteran of World War II; on the staff of Greens' Eye Hospital; chief, department of ophthalmology, Kaiser Foundation Hospital, where he died Jan. 13, aged 56.

Slosser, Dyle Jason Ⓜ Defiance, Ohio; Starling–Ohio Medical College, Columbus, 1913; member of the House of Delegates of the American Medical Association in 1946; since 1945 coroner of Defiance County; past-president of the Ohio Coroners Association and the Defiance County Medical Society, which he also served at one time as secretary; formerly secretary of the Northwestern Ohio Medical Society; member of the American Academy of General Practice; served during World War I; on the staff of the Defiance Hospital; died Jan. 15, aged 75.

Snyder, William Joseph Kline Ⓜ Avalon, Pa.; Bellevue Hospital Medical College, New York City, 1895; served as president of the school board; for many years associated with the Suburban General Hospital in Bellevue, which he helped organize; a founder, and for many years president and chairman of the board, Avalon Bank; died Jan. 20, aged 94.

Spinner, Samuel Leonard Ⓜ Elizabeth, N. J.; L.M.S., & M.A.S., England, 1917; veteran of World War I; on the staff of the Newark Beth Israel Hospital; died in Elizabeth General Hospital Jan. 20, aged 68.

Stangland, Arthur K. Ⓜ Highland, Ind.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; associated with the West Surburban Hospital in Oak Park, Ill.; died Jan. 27, aged 78.

Staniford, Kenneth Jamison Ⓜ Bass Lake, Calif.; Cooper Medical College, San Francisco, 1911; past-president of the Fresno County Medical Society; served on the Fresno County Board of Health; was a member of the city parks commission; veteran of World War I; died Jan. 25, aged 69.

Stauffer, Leslie John Ⓜ Bothell, Wash.; Northwestern University Medical School, Chicago, 1910; member of the American Academy of General Practice and the Industrial Medical Association; formerly associated with the Indian Service; died Jan. 19, aged 74.

Stayton, Howard Nehemiah Jr. Ⓜ Newark, Del.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1940; plant physician of the Chrysler Corporation for seven years; formerly member of the state board of health; at one time practiced in Lewes, where he served on the staff of the Beebe Hospital; died Jan. 23, aged 44.

Stoumen, Samuel Ⓜ Bethlehem, Pa.; Maryland Medical College, Baltimore, 1911; served as deputy coroner of Northampton County; on the staff of St. Luke's Hospital, where he died Feb. 4, aged 71.

Swanson, Cleary Neil Ⓜ Detroit; Harvard Medical School, Boston, 1923; clinical assistant professor of obstetrics and gynecology at Wayne University College of Medicine; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; past-president of the Michigan Society of Obstetricians and Gynecologists and the Michigan Obstetrical Society; associated with the Highland Park (Mich.) General Hospital; for many years head of the department of obstetrics and gynecology at Mount Carmel Mercy Hospital, where he died Jan. 21, aged 61.

Swinney, Roy Goldson, Richland, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1905; past-president of the Keokuk and Jefferson Counties Medical societies; for many years member of the school board; for a time chief of the medical staff at the Jefferson County Hospital in Fairfield; during World War II served in the state guard; died in the Ottumwa (Iowa) Hospital Jan. 2, aged 77.

Thompson, William Augustas Ⓜ Citronelle, Ala.; University of Tennessee Medical Department, Nashville, 1904; member of the American Academy of General Practice; served as mayor; died Jan. 21, aged 75.

Tint, Louis Jacob Ⓜ Chicago; Jefferson Medical College of Philadelphia, 1908; member of the American Academy of General Practice; veteran of World War I; died in the Albert Merritt Billings Hospital Feb. 3, aged 79.

Vail, George Francis, Hartford, Conn.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; associated with McCook Memorial and St. Francis hospitals, and the Hartford Hospital, where he died Jan. 8, aged 80.

Vassey, Thomas, Trenton, N. C.; University of Tennessee College of Medicine, Memphis, 1938; served an internship at the Norfolk General Hospital in Norfolk, Va., and a residency at the Leigh Memorial Hospital in Norfolk, Va., died Jan. 1, aged 47.

Ward, Edward, Flushing, N. Y.; Jefferson Medical College of Philadelphia, 1923; served on the staff of the Flushing Hospital; died Jan. 5, aged 59.

Webb, Byford Hodgen Ⓜ West Frankfort, Ill.; St. Louis University School of Medicine, 1906; veteran of World War I, serving with the American Expeditionary Forces in Europe; died in the Franklin Hospital, Benton, Jan. 21, aged 77.

Webster, Howard Hamilton, Dayton, Ohio; Hahnemann Medical College and Hospital of Philadelphia, 1903; died Jan. 24, aged 78.

Whitmore, William Harvey Ⓜ Captain, U. S. Navy, retired, Norfolk, Va.; University of Virginia Department of Medicine, Charlottesville, 1916; entered the Navy in 1917 and retired July 1, 1938; veteran of World Wars I and II; past-president of the Radiological Society of Virginia; on the staffs of the Norfolk General and De Paul hospitals; died Jan. 30, aged 66.

Woodward, Lee Roy Ⓜ Mason City, Iowa; Rush Medical College, Chicago, 1917; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Iowa State Medical Society; on the staff of the Park Hospital, where he died Dec. 9, aged 73.

FOREIGN LETTERS

BRAZIL

Tuberculous Meningitis.—João Batista dos Reis and co-workers of the University of São Paulo (*O Hospital*, vol. 55, January, 1959) compared the results of treatment in 14 patients who had tuberculous meningitis with those in an earlier series of 16 patients who were successfully treated with systemic and intrathecal doses of streptomycin. In the earlier series spinal fluid examinations were performed monthly during the whole treatment. None of the patients developed serious neurological or psychiatric complications. In the later series, in addition to streptomycin, the patients were given isoniazid and ACTH. In the second group the fibrin clot was absent from the spinal fluid in the 6th month as compared to the 14th month in the first group; the cell count became normal in the 8th month as compared to the 14th month in the first group; the protein level became normal in the 5th month as compared to the 10th month in the first group; and the sugar level became normal in the 4th month as compared to the 6th month in the first group. These findings demonstrated the value of adding isoniazid and ACTH to the therapeutic regimen.

DENMARK

Ornithosis-Related Antigens.—Soluble ornithosis-related antigens were obtained from 22 of 30 strains of Bacillus anitratum by Volkert and Matthiesen (*Acta path. et microbiol. scandinav.* **44**:278-286, 1958). Antigen-antibody analyses with these antigens and five representative human ornithosis serums revealed certain differences in both the quality of the antigens and the antibodies. Ornithosis antigens and antigens from selected bacterial strains were tested against 172 human ornithosis serums, and 96% of the serums gave positive complement-fixation tests with all antigens. In 89% equal antibody titers were obtained. The ornithosis-related antigens were also tested with 500 ornithosis-negative serums originating from patients suffering from acute infectious diseases. Of these 3% gave positive complement-fixation reactions with the bacterial antigen only. The problem of false-positive serum reactions due to the use of B. anitratum antigen in the diagnostic tests for ornithosis is still unsolved, and until this has been investigated further the practical value of the B. anitratum antigen cannot be determined.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Vitamin B_{12} Deficiency in Anemia.—Determination of the vitamin B_{12} level in plasma was performed on 40 patients with uncharacteristic macrocytic anemia, whose marrow did not contain typical megaloblasts but a varying number of large erythroblasts or macroblasts and who exhibited, in most cases, maturation disturbances of the myelopoietic system in the form of large metamyelocytes and large hypersegmented neutrophils. This was reported by Kristensen and Gormsen (*Acta med. scandinav.* **162**:415-422, 1958). Abnormally low plasma concentrations of the vitamin were common among these patients. Broadly speaking, there was agreement between the degree of the marrow changes and the plasma vitamin B_{12} level, abnormally low levels being found in all patients whose marrow contained numerous giant cells, whereas among the group whose marrow contained only occasional giant cells the level was abnormally low in some and normal in others. Patients with a low plasma vitamin B_{12} concentration responded to parenteral administration of the vitamin.

The study showed that low vitamin B_{12} levels in the plasma, reflecting a deficiency of the vitamin, might be present although the marrow revealed no cells that could be definitely designated as megaloblasts. This supported the assumption that the finding of large metamyelocytes and hypersegmented neutrophils (pernicious anemia neutrophils) in the marrow may be an early histological sign of pernicious anemia. The authors pointed out the significance of being able to make a diagnosis of vitamin B_{12} deficiency before typical changes have appeared in the blood or marrow.

Reserpine for Hypertension.—A. R. Krogsgaard (*Acta med. scandinav.* **162**:449-463, 1958) used reserpine to treat 75 patients with benign essential hypertension, the maintenance dose being about 0.5 mg. daily in most cases. In 39 of these treatment was supplemented later by hydralazine, the maximum dose being 400 mg. daily. To elucidate the frequency of the initial side-effects of hydralazine with and without preceding administration of reserpine, 24 patients were treated with hydralazine alone. Reserpine as the only form of treatment gave a satisfactory result (fall in the mean blood pressure of 20 mm. Hg at least and of 140 mm. Hg at most, and abatement of reversible eyeground changes) in 11 of 75 patients. In these 11 patients the blood pressure fell on the average from 209/123 to 161/93 mm. Hg. When a placebo was given after an average duration of treatment

of 15.7 months, the mean blood pressure rose by 20 to 37 mm. Hg in six patients but did not change significantly in the remaining five.

Most of the patients who responded satisfactorily to reserpine alone had a less severe hypertension than the others in the series. When reserpine was given prior to and simultaneously with hydralazine fewer side-effects of the latter were seen, and more patients were able to complete the treatment. Furthermore a more rapid rise in the dose of hydralazine became possible. Of the 39 patients treated with reserpine and hydralazine 20 completed the treatment satisfactorily. In these patients the blood pressure fell on the average from 225/127 to 181/97 mm. Hg. When a placebo was given after an average period of combined treatment of 29.5 months, the mean blood pressure rose by 20 to 24 mm. Hg in three patients, by 10 to 19 mm. Hg in eight, and did not change significantly in the remaining nine.

The authors concluded that reserpine as the only form of treatment produced a satisfactory result in a small proportion of patients with benign hypertension, chiefly in the milder forms. In the rest of the patients reserpine might form a valuable basis for combined treatment with hydralazine. After prolonged treatment the administration of reserpine might be tentatively discontinued, as about half the patients would then be able to dispense with this drug.

In the same issue Krogsgaard described the side-effects of reserpine in 36 patients treated with reserpine alone and 39 treated with reserpine combined with hydralazine. Side-effects of reserpine treatment occurred in 60 of the patients. They were insignificant in most cases (nasal congestion, diarrhea, and fatigue) and tended to subside with continued treatment, but in 20 patients treatment had to be discontinued because of edema or other undesirable side-effects. A weight gain occurred in 26 patients amounting maximally to 16.8 kg. (37 lb.) and averaging 7.2 kg. (16 lb.). In only one patient did the increase in weight necessitate discontinuance of treatment. In the course of continued treatment the weight fell again in some of the patients and after cessation of the treatment in most. Mental depression was the severest side-effect, seen in 13 patients. Treatment with reserpine was discontinued in 12 of these. In one patient the mental depression led to suicide. Two patients had to be admitted to psychiatric wards and one of these committed suicide one year later. The patients who developed mental depression had a higher frequency of previous depression than the other patients or had a familial predisposition to this. The dose of reserpine given to the depressed patients often exceeded 1 mg. daily. Pronounced depression in a patient or in his family constituted a contraindication to ambulant treatment with reserpine.

Occupational Allergy.—From 1944 to 1956 4,348 allergic patients suffering from bronchial asthma, vasomotor rhinitis, or angioneurotic edema were examined at the Allergic Clinic, Copenhagen, by Bruun and Lorenzen (*Acta allergol.* **12**:432-440, 1958). The authors assumed the following criteria for allergic diseases of occupational origin: (1) the allergic disease must not have been present prior to the work that is considered injurious, (2) the symptoms must chiefly appear during work and always be most pronounced at the place of work, and (3) the patient's condition must improve materially when he is off duty for prolonged periods as, for instance, during holidays. Judging by these criteria 281 patients (6.5%) were found to be suffering from occupational allergy.

New Succinimide for Epileptics.—Trolle and Kiørboe (*Nord. med.* **60**:1780-1782 [Dec. 11] 1958) treated 38 patients who had petit mal seizures with PM 680 for periods averaging eight months; 14 became seizure-free, 17 had 50 to 99% reduction in seizure frequency, and 7 showed no improvement. Thirty patients had typical petit mal seizures and only three of these did not react to the treatment. Of six patients with myoclonic fits two became seizure-free, two had clinical improvement, and two did not respond to treatment. Two patients with atypical loss of consciousness showed no improvement. The drug was not given to patients with typical psychomotor epilepsy. In several patients it was found to be superior to both phensuximide and oxyphenbutazone, and side-effects were less frequent.

Treatment of Necrotic Lesions.—Storm and Hilmer-Nielsen (*Nord. med.* **60**:1831-1834 [Dec. 18] 1958) used stabilized crystalline trypsin as a powder aerosol on 10 patients with large necrotic lesions and observed a rapid resolution of the necrotic tissue in five or six days. It was impossible to say anything about the course of illness in these patients if the lesions had been treated by other means, but in most of the patients other treatments had been tried without benefit before the trypsin therapy. The two patients in whom the trypsin therapy partially failed had extremely low healing tendencies because of their poor general condition and local nutritional disturbances.

Serum Transaminase Activity.—In 120 patients serial determinations of serum glutamic oxalacetic transaminase and glutamic pyruvic transaminase levels were made and reported on by Ersbak (*Nord. med.* **61**:49-54 [Jan. 1] 1959). The possibilities of a more differentiated clinical interpretation were examined on the basis of the curve patterns. The serial determinations of the two transaminases simultaneously demonstrated characteristic changes diagnostic of coronary infarction, metastases to the

liver, chronic liver disease, acute parenchymatous liver disease, and occlusive liver disease. Although variations from the characteristic pattern might be seen, serial determinations of the activity of the transaminases were considered to be of greater value than single determinations.

Rubella and Pregnancy.—There has been a marked rise in the incidence of rubella in Denmark. In the period 1950-1952 about 6,000 cases were reported and in 1955, there were 54,815. Because of the risk of malformations in children whose mothers had had rubella at an early stage of their pregnancies, Jacobsen and Christensen of the Odense general hospital (*Ugeskrift for læger*, Jan. 8, 1959) sent a questionnaire to physicians to ascertain the frequency of such malformations. They found that 43 pregnancies had been complicated by rubella, and that among the 32 women whose rubella had occurred within the first 16 weeks of pregnancy 19 had given birth to healthy children and 8 had aborted. In several cases confinement had been normal, but the infants presented such malformations as heart disease, cataract, or defective dental enamel.

Among the 23 women for whom abortion had been induced on account of rubella, 5 had wished to have a child but had been so alarmed by the prospect of malformations that they wished to sacrifice it. Among the 5,400 abortions induced in Denmark in 1955 there were 406 for whom this was done on account of rubella. Jacobsen and Christensen concluded that if rubella occurs in the early months of pregnancy, and if the mother desires the termination of her pregnancy on this account, this wish should be granted. They suggested that, in order to get more statistical information on the subject, under the heading "rubella" in the weekly list of reportable diseases there should be a subheading to be filled in with the coincidence of pregnancy and its duration at the onset of the rubella.

Cancer of the Rectum.—In the 10-year period 1946-1955, there were 180 cases (112 in men and 68 in women) of cancer of the rectum in Aarhus (population of 113,000). These cases were reported on in the *Danish Medical Bulletin* for December, 1958, by Dr. N. Blixenkrone-Möller who calculated that these cases represented an average of one such case per year for every 6,280 persons. Up to the age of 60, the disease was equally distributed between the sexes, but after this age there was a steep rise in men but not in women. In 70% the tumor was situated at most 10 cm. above the anus and could therefore be reached by the exploring finger.

Among the 170 patients whose tumors were examined microscopically, 158 tumors were adenocarcinomas, 6 were solid carcinomas, 5 were malignant papillomas, and 1 was a lymphosarcoma. The tumors were regarded as inoperable in 55 of the total instances and as operable in the remaining 125. Major operations were performed in 78%. Five years after the diagnosis, 31% of the operable patients were still alive. Of the operable patients who underwent rectal resection, 37% were alive five years later. The prognosis proved to be better for those whose symptoms had existed for more than three months than for those with an interval shorter than three months. The author concluded that it was desirable to use a more extensive removal of pelvic connective tissue and perineal skin that has so far been the practice, especially in low-level cancers of the rectum.

Artery Transplantations.—At a meeting of the Jydsk Medicinsk Selskap, reported in *Nordisk medicin* for Feb. 12, Jakobsen and co-workers reported a series of 41 patients on whom arteries had been transplanted at the Aarhus general hospital since 1955. They had been selected from among the 97 patients subjected to arteriography with the possibility in mind of transplantation for the relief of intermittent claudication, pain, necrosis, or gangrene. Most of them had arterial obstruction of the lower limbs, but nine had such an obstruction of the abdominal aorta. In 7 the symptoms had existed for less than six months, and in 14 for over five years. Most were between the ages of 50 and 60, and one was over 80. The grafts had been taken from the young and healthy victims of fatal accidents, seldom more than six to eight hours after death. Among the 38 survivors of the transplantations, 31 were cured or much improved, but, until the complication rate can be effectively reduced, the indications for transplantation must be imperative, the mere arteriographic demonstration of an obstruction being no call for it in the absence of symptoms.

Public Health Data.—Dreyer and Frandsen (*Danish Medical Bulletin*, January, 1959) reviewing the statistical reports for 1956 and 1957 found that the behavior of the reportable diseases was rather erratic, with an increase in influenza from 115,203 in 1956 to 544,613 in 1957. On the other hand the incidence of poliomyelitis fell from 191 (37 paralytic and 154 nonparalytic) in 1956 to 26 (10 paralytic and 16 nonparalytic) in 1957. In neither year was a single case of diphtheria reported. Since 1954 there has been a slight fall in the incidence of gonorrhea, but the figure for 1957 of 7,447 cases is relatively high. About half this number were reported in Copenhagen. The infant mortality continued to fall with 25.2 deaths per 1,000 live births in 1955 and 23.4 in 1957. The two leading causes of death, malignant growths and degenerative cardiovascular disease, accounted for 46% of all the deaths in 1957. The tuberculosis mortality was down in this year to 4.4 per 100,000, with pul-

monary tuberculosis accounting for 3.8 per 100,000. The deaths from all forms of tuberculosis amounted to less than a third of the deaths from traffic accidents. There are now 10.15 hospital beds available per 1,000 population, and there is one practicing physician for every 864 of the total population.

Complications of Blood Transfusion.—At the Slagelse general hospital Dr. S. A. V. Jörgensen (*Ugeskrift for læger*, Jan. 22, 1959) investigated the frequency with which transfusion from a blood bank is followed by nonhemolytic reactions as tested by measurements of the temperature of the recipients before and after this operation. During the three-year period 1954-1957, 2,173 of the 4,223 transfusions were controlled by such measurements immediately before and half-hourly for three hours after a transfusion. The reaction was uncomplicated in 67.4%, febrile in 31.1%, and allergic (urticaria or angioneurotic edema) in 1.5%.

When the 233 febrile temperatures before transfusion were subtracted from the total of 677, there remained 444 (or 20.5%) which could be traced to the transfusion. Most of these could be dismissed as trivial, but 3 or 4% with a febrile reaction severe enough to call for preventive measures remained. No alteration in the incidence of reactions was observed after the introduction of infusion apparatus for use only once, but the author is exploring the effects of a routine addition of antihistamine to the blood immediately before a transfusion. Meanwhile the chief merit of the present study has been its demonstration of the great uncertainty over the underlying causes of the reactions to blood transfusion and how to prevent them.

FINLAND

Drug Addiction and Crime.—Westling and Riippa (*Ann. med. int. Fenniae* 47:205-222, 1958) investigated the criminal record of 169 drug addicts (107 men and 62 women) treated at some of the mental hospitals of Helsinki. Of these patients 75% of the men and 40% of the women had committed, at some time in their lives, at least one crime for which they had been sentenced. In a control group made up of men, the corresponding figure was 16.4%. Among persons who had become addicted before the war there was no primarily criminal patient, whereas among those who had become addicted after the war the percentage who were primarily criminals was 42% for men and 15% for women. Both of these groups contained a large number of persons who had committed crimes after having taken to drugs. For the postwar male group the figure was 78%. The crimes that increased after addiction were primarily theft, fraud, smuggling, and forgery. On the other hand, the number of violent acts remained practically unchanged. The number of these persons who had committed acts of violence must, however, be considered exceedingly high (about 20% of the men). About 60% of primarily noncriminal addicts committed some crime in the course of the eight years after addiction. Among physicians who had become addicts the percentage committing crimes was far below the average. Primary as well as secondary criminality attained the higher figures, the younger the persons were when they became addicted to drugs. The more accidental the reason for addiction, i. e., the more powerfully it had been motivated by a desire for euphoria, the more accentuated was the criminality.

Reserpine and Vascular Changes Caused by Smoking.—Experiments with 18 healthy subjects confirmed that smoking one cigarette increased the heart rate and the systolic blood pressure and decreased the cutaneous temperature of the foot. Iisalo and Kärki (*Ann. med. exper. et biol. Fenniae* 36:343-349, 1958) gave these subjects 1.0 to 1.5 mg. of reserpine a day for three or four days and observed that smoking increased the heart rate and lowered the cutaneous temperature significantly less under reserpine treatment than in the control experiments without reserpine.

Methanol Poisoning.—A. R. Alha and co-workers (*Ann. med. exper. et biol. Fenniae*, 36:444-455, 1958) attempted to ascertain whether in forensic practice it would be possible to use the determination of formic acid in brain, kidney, liver, and blood as a criterion of methanol poisoning, if no urine was available. In the estimation of formic acid, distillation in steam was used for the isolation and the oxidative reaction with mercuric chloride for the determination, the yield of mercurous chloride being measured gravimetrically. The yield was found to be 70 to 90% in the urine, brain, and kidneys. By contrast, the liver and, in particular, the blood gave smaller yields. In addition, "normal" formic acid concentrations were found to be 5 mg. or less per 100 Gm. In 10 fatal cases of methanol poisoning the formic acid concentration in the organs examined was markedly higher than "normal." In all cases methanol was qualitatively demonstrated in a steam distillate of mixed viscera. This investigation showed that for the detection of acute methanol poisoning it was often sufficient in forensic medicine, when methanol had been qualitatively detected in the body, to prove that the concentration of formic acid was increased in the urine or, if urine was not available, in the viscera, preferably the brain or kidneys.

Smoking, Serum Cholesterol, Blood Pressure, and Obesity.—Keys and Brozek, with the collaboration of Finnish workers (*Lancet* 1:492, 1959), examined the effect of cigarette smoking on serum cholesterol

levels, blood pressure, and obesity in 360 male smokers and 165 male nonsmokers in Helsinki and the rural districts of west and east Finland. They reported that in all regions and in all age groups, except in those aged 50 to 59 in west Finland, smokers had a higher average serum cholesterol level than nonsmokers. Among smokers those who smoked most tended to have the highest serum cholesterol level. At all ages and in all regions in Finland smokers tended to have slightly lower blood pressures than nonsmokers, although the difference between them was small. In both rural areas the smokers tended to be slightly thinner than the nonsmokers, although in Helsinki there was no clear relation between smoking and obesity. The authors pointed out that their data did not explain the origin of the differences in serum cholesterol levels, blood pressure, and body fat. They could not, therefore, conclude that habitual cigarette smoking caused the serum cholesterol level to rise, the blood pressure to fall, or the body to lose fat. Brozek and Keys in another study found that men who stopped smoking tended to become fatter, an observation in keeping with the general view that smoking curbs the appetite.

NETHERLANDS

Diabetic Survey.—J. D. Mulder and E. van de Weg (*Huisarts en Wetenschap*, p. 66, December, 1958) made a survey for undetected diabetes in three districts with a total population of about 31,700. The preliminary screening was made with Clinistix and, if glycosuria was suspected, a glucose tolerance test was made. In one district (about 10,000 people) 0.41% were found to have undetected diabetes. In the second district (about 14,000 people) the percentage was 0.22, and in the third (7,700) it was 0.19. The wide variation of the percentages obtained in these three districts might be due partly to analytical errors made in districts 2 and 3. On the whole, however, these figures are much smaller than those reported in other countries. Of the 88 patients whose diabetes was thus detected, 3 were between the age of 20 and 40; 32 were between 40 and 60; and 53 were over 60. In most the diabetes was mild but in 31 the fasting blood sugar level appeared to be more than 300 mg. per 100 ml.

The Reliability of the Differential Leukocyte Count.—C. L. Rümke and C. van Eeden (*Nederl. tijdschr. geneesk.* 102:2505, 1958) discussed the reliability of the differential leukocyte count. They first considered whether the smears were correctly made. The variability can be calculated statistically. When, for example, the blood contains 4% band-form neutrophils, the percentage found by counting 200 cells will vary in 95% of cases between 1 and 8%. In the remaining 5% a much larger deviation may be encountered. This variation will depend on the percentage present in the blood of the type of cells counted and on the total number of cells counted. By counting 200 cells of blood which contains 50% lymphocytes, the variability will be in 95% of cases between 39 and 61%. By counting 1,000 cells, this variation will be 46 to 54%. Mostly, however, the physician will be interested in the opposite: what is the reliability of the figures obtained? It is impossible to give exact figures, but it is possible to find 95% confidence limits. When 200 cells are counted and none of one type of cell is found, this means that up to 4% of that type of cell may be present. When 5% are found this means that from 1 to 12% may be present. For 10%, these figures are 4 and 18; for 25%, 16 and 35; and for 50%, 39 and 61.

Hemolytic Streptococci in Children.—H. C. Zanen and S. Wagenaar (*Nederl. tijdschr. geneesk.* 102:1198, 1958) investigated the prevalence of group A hemolytic streptococci in healthy inmates of a children's home. The children, ranging from 2 to 7 years, were examined fortnightly over a period of two years. On the average 50% of the tests were positive. In the summer only a few children (about 2%) appeared to be infected. In the winter at times up to 100% of the tests were positive. In the two-year period there were seven epidemics, all of which were caused by different strains. On the average, 10% of the new infections were attended with illness. Each child had about three subclinical infections with a new type of the group A hemolytic streptococcus annually. In only two instances was a new infection observed with the same strain within four months. On the average each child had suffered every three or four years from a streptococcic illness.

Type 14 caused all of the 3 cases of scarlet fever and 7 of 13 other streptococcic illnesses observed in these children. This type was found in 40% of the 510 patients with scarlet fever who were treated in Amsterdam during the same period. This suggests an increased pathogenicity for this strain at the time of this investigation. In two children illness was caused by type 28; in two by type 12; in one by type 4/26; and in one by type 1. In view of the repeated occurrence of group A hemolytic streptococci in children, a positive culture is not believed to be of much clinical significance. The use of penicillin against streptococci should be limited to severe clinical infections and to the prevention of recurrent rheumatic fever. No purpose is served by keeping healthy carriers home from school.

A New Periodical.—In November, 1958, a new periodical, *Spreekuur thuis* (The Doctor at Home), made its appearance. It is issued by the Netherlands Medical Association to give the lay population information about health and medical science. The editor called attention to the increasing desire of

the people to be fully informed about such problems. In view of the importance of good and reliable information, the association thought it wise to issue a magazine to which many specialists would contribute.

SWEDEN

Armchair Treatment for Cardiac Infarction.—Sture Helander (*Acta med. scandinav.* **162**:351-359, 1958) reported on one series of 112 patients treated in an armchair and given anticoagulants and another series of 100 patients treated in an armchair without anticoagulants. In the first group the mortality was 10%, compared with 15% in the second group. A third series of 80 patients was treated with rest and anticoagulants, with the resulting mortality of 26%. The aim of the armchair treatment was not to increase the effort of the patients, but, on the contrary, to ease the burden of the heart muscle. The distribution of cases of cardiac infarction with regard to their severity was reasonably comparable in all three groups, with a somewhat lower percentage of severe cardiac infarction in the armchair group receiving anticoagulants. Most of those who died showed ominous prognostic signs such as arrhythmia or heart block. About half of the patients had had one previous attack of cardiac infarction as shown at autopsy. Of the 25 patients who were treated in an armchair and who died, 14 had had previous attacks. The frequency of embolic complications was negligible in all groups and was not thought to have had any effect on the issue. Armchair treatment seemed to constitute a good prophylactic measure against embolic complications and it seemed probable that it was sufficient to treat only the bad prognostic risks (those with arrhythmias, heart block, and cardiac failure) with anticoagulants.

Subarachnoid Hemorrhage.—Olle Höök (*Acta med. scandinav.* **162**:475-492, 1958) reported a series of 152 patients who had subarachnoid hemorrhage and who were admitted within no more than one week after the hemorrhage. More than 90% were admitted in the first or second day of illness. The author suggested the classification of the patients in special risk groups, thereby greatly increasing the possibility of comparing material from different investigations. He also pointed out that patients with subarachnoid hemorrhage from different hospitals could not be considered congruent entities from the prognostic point of view even though, on the whole, they might be of the same degree of severity because such factors as age and treatment might vary according to the type of hospital. The mortality was highest on the first day, had decreased appreciably after the first two weeks, and was much lower after eight weeks. In from 10 to 15% of the patients the cerebral damage caused by the hemorrhage was of such magnitude that most were beyond help from any kind of therapy. The late prognosis was much better for the groups operated on than for those treated conservatively.

In the same issue Olle Höök reviewed a series of 138 patients with subarachnoid hemorrhage in which no aneurysm was revealed by angiography. Of these patients, 136 were followed for an average of 4.5 years. The average age at the time of admission to the hospital was 43 years and the sexes were evenly divided. The symptoms were usually relatively mild and 67% of the patients presented no focal neurological signs. The late prognosis with respect to recurrent fatal hemorrhage was favorable, with an incidence of 6%.

Causes of these hemorrhages were varied. With few exceptions, the investigations were complemented with vertebral angiography if the symptoms indicated that the basilar region was involved. In isolated cases arterial aneurysms may completely thrombose, making it impossible to trace them angiographically. In some patients a primary intracerebral hemorrhage appeared to have occurred with penetration of the hemorrhage into the ventricular system and/or to the surface of the brain in the subarachnoid space. This accounted for only 7% of the present series, however. The possibility of spinal subarachnoid hemorrhage, which is often difficult to distinguish from intracranial bleeding, should be considered. If the pain is initially localized in the back and radiates to the arms or legs, there is a fair possibility of spinal hemorrhage. Spinal subarachnoid hemorrhages usually arise from vascular tumors and malformations but are occasionally associated with other types of tumor such as sarcoma, ependymona, and neurinoma.

In suspected vascular malformations in the cervical and upper thoracic spinal cord, vertebral angiography may give valuable information. Vertebral angiography is indicated in subarachnoid hemorrhage when bilateral carotid angiography fails to show any source of the bleeding (1) if there are any neurological symptoms from the vertebral-basilar region, (2) in young patients, and (3) in recurrent hemorrhages. In this series 10 of the patients died. Autopsy, performed on five of these, revealed arterial aneurysms in two. One of these aneurysms was situated on the basilar artery and had not previously been visualized in the angiogram.

Spondylolisthesis.—The relationship between the lesions and the symptoms in spondylolisthesis was studied by Gösta Kollberg (*Nord. med.* **60**:1778-1780 [Dec. 11] 1958) who stated that disk degeneration, rupture of a disk, and narrowing of the intervertebral foramina have one factor in common which could produce an increase in the symptoms, namely, abnormal mobility (instability) between the vertebrae. In a series of patients with spondylolisthesis

of L_5 and S_1, the instability of L_5 and S_1 did not markedly influence the degree of severity of the subjective symptoms.

Burns.—Gunnar Birke and co-workers (*Nord. med.* 60:1824-1828 [Dec. 18] 1958) stated that an extensive burn could not be regarded as a lesion involving the skin only. It causes pathophysiological disorders in the whole body and is often accompanied by severe bacteriological complications. After an extensive burn large amounts of albumin are lost from the circulation, particularly in the early phase. There is also an abnormal distribution of albumin in the body, with accumulation of albumin especially in the subcutaneous tissue. In the first 24-hour period there is, in addition, hemoconcentration, increased destruction of blood cells, hyperkalemia, and acidosis. Later the hyperkalemia is often succeeded by hypokalemia. The sodium content of the blood varies from patient to patient, depending on the manner in which the fluid replacement is carried out. Urinary excretion of histamine, epinephrine, levarterenol, and corticosteroids is greatly increased at first and, excepting that of histamine which is normalized in 24 to 48 hours, it remains raised throughout the first week.

Cardiac catheterization was performed in a number of patients and in shock it provided valuable information to aid the differential diagnosis between hypovolemic shock and primary cardiac insufficiency. The tendency to pulmonary edema, which is present during the so-called absorption phase, does not seem to be associated with heart failure, but is probably a manifestation of capillary damage in the lungs, with a change in permeability on the basis of a direct burn or, possibly, caused by humoral factors or infection. Bacteriological studies have shown that in cases of infection in the skin lesions the first symptoms appear as a rule after the second day, and that staphylococci and gram-negative rods are the most important causative agents. Infections resistant to treatment and due to bacterial strains occurring in the hospital play a predominant role in these patients. In about 50% of those who die, infections, mainly in the form of bronchopneumonia and sepsis, are a contributory cause of death.

In the same issue these authors stated that during the acute phase in the course of extensive burns, intravenous replacement therapy is essential to prevent hypovolemic shock. Dextran is an excellent plasma expander, but in third degree burns involving more than 20% of the body surface whole blood should also be given and, if possible, albumin as well. Sodium bicarbonate and glucose should also be given at first. After 48 hours the sodium intake should be restricted and potassium given instead. Oxygen inhalations combined with careful checking of the ventilation is important in patients with pulmonary complications. Antihistamines should be given, but corticotropin is rarely indicated. Measures to prevent infection are important and should include isolation of the patient and treatment under aseptic conditions. When infection occurs, bacteriological examination with determination of antibiotic resistance should first be made. Antibiotics should be given in an adequate dose, preferably by the intravenous route. Excision and skin grafting of third degree burns should be performed as early as possible. The importance of centralization of the treatment of burns in a special center is stressed.

Sideropenia.—Ian Lundholm (*Nord. med.* 61:7-13 [Jan. 1] 1959) reported on a follow-up of 123 patients with hypochromic anemia of whom 117 were women. These patients were first seen in 1939. Two patients had developed cancer of the hypopharynx and one a sublingual cancer, which was cured. Of 80 who died one had cancer of the esophagus. The incidence of recurrence was high. Of the entire series 60 patients had a total of 142 relapses. The more severe ones were induced by acute causes, especially hemorrhage. Restoration to normochromia occurred only gradually with increasing age, probably indicating a slow building up of the depot iron. The irreversibility of the symptoms of sideropenia was higher in the patients who initially sought medical advice for their anemia only and in those who were traced secondarily through family members than in the rest who were incidentally discovered to have the disease. This was interpreted as evidence of a constitutional hereditary factor. A similar clinical course in three pairs of monozygous twins gave further support to the hypothesis advanced in 1939 that a dominant gene determines the tendency to inadequate absorption of iron, a tendency that is revealed in particular when large amounts of iron are lost by hemorrhage.

It was observed that 10.6% of all the patients and 26% of those with stationary achlorhydria had an acquired pernicious anemia. The incidence of this condition in the normal population is about 0.2%. Membranes in the hypopharynx were found in 20 patients. These were considered as especially disposed to cancer. The membranes were more resistant to iron therapy than were the other manifestations. Animal-protein deficiency was found in 38% of the patients at the initial examination but in only 10% of those followed up. Only a few showed a marginal intake of iron at the initial examination. Hereditary factors, marginal intake of iron in the food, and pathological bleeding have in adolescent girls been found likely to give rise to sideropenia, which will then recur with any slight extra demands on the iron depots.

Cholecystokinin in Cholecystography.—Tomenius and Backlund (*Nord. med.* 61:41-47 [Jan. 8] 1959) stated that preparations of cholecystokinin (CCK) corresponding to 0.04 mg. of substance per kilogram

of body weight, a total of 3 mg. in adults, were injected intravenously in 650 patients in connection with cholecystography. Contraction of the contrast medium-filled gallbladder and visualization of the bile duct was produced within 2 minutes, with a maximum after 15 to 20 minutes. In a series of 59 patients, the effect of the cholecystokinin test was compared with that of the egg-yolk meal, both tests being performed on these patients. The former test was found to be superior to the egg-yolk meal in that it saved time and was more reliable, particularly for visualizing the cystic duct and common bile duct. In 8 of the 59 patients the contrast medium-filled gallbladder did not respond to either stimulant. The CCK test was found to reduce the time necessary for cholecystographic analysis to one-fourth of that required by the egg-yolk meal. No severe side-effects were noticed. A further analysis of 612 patients who were examined later was made, and the phenomenon of good contrast medium filling without any visible stones combined with poor contraction of the gallbladder was also reported. A roentgenologic examination of the stomach can be made at the same time. Stones of the ductus choledochus were evacuated during cholangiography in one patient with CCK.

Ataraxics for Mental Patients.—In 1957 Bo Rydberg (*Nord. Med.* **61**:93-95 [Jan. 15] 1959) started using ataraxics in treating 26 patients who were extremely dangerous to other persons in a maximum security pavilion. Such a pavilion requires special technical safety arrangements and a big nursing staff. Chlorpromazine, reserpine, perphenazine, and other drugs alone or in combination were used. After determining the maintenance dosage in each case, the patients were treated for 6 to 12 months. The results of this treatment were classified as not improved, distinctly improved, much improved, and greatly improved. Greatly improved meant that the patient could be kept in an ordinary mental hospital. Of these 26 patients 4 were in this category, 11 were much improved, 10 distinctly improved, and 1 not improved. One patient was actually transferred to an ordinary mental hospital and was working regularly when last observed. As a result of treatment the tension in the pavilion was greatly reduced. This was a relief to the staff and might even allow a reduction in their number.

Dystocia Eased by Vacuum Extractor.—O. G. A. Berggren (*Svenska läk.* **51**:3715-3732, 1958) at the Linköping Obstetrical Clinic used a Malmström vacuum extractor as a substitute for forceps in difficult labor. Although the principle of the extractor had been known since the 18th century, it was only with the modification invented by Dr. Malmström in 1956 that any truly superior results were gained with it as compared with those when the forceps was used. Swedish experts believe that the use of the new instrument will reduce the number of cases of cerebral palsy. Two groups of women delivered with forceps and their children were studied and compared with a group of suction-delivered patients, a total of 150 deliveries. Not only was the new method more gentle on the child but also it speeded up labor and gave rise to far fewer serious perineal tears (26% perineotomies as against between 83 and 94% with forceps) or other complications.

As a rule the operation was over in a few minutes and the average postdelivery time was reduced to 8.7 days as compared with 12.7 days when a forceps was used. Vacuum extraction was suitable also as a substitute for certain types of cesarean section. An additional advantage is the possibility of reducing the delivery staff for, as opposed to the forceps method, the use of the Malmström instrument requires no anesthetization. The vacuum extractor on the contrary acts as a stimulus on the natural labor contractions. The synchronous application of the vacuum power and the voluntary labor movements of the mother make it possible to arrive at a process which more nearly approaches physiological delivery. This in turn, gives the child's head a chance to recover from the strain of passing through the birth canal. The Malmström instrument has all-metal suction cups. There are three sizes so as to permit reaching the head even when it is arrested in the upper sections of the pelvis. This is another clear advantage over forceps, which are difficult to apply in patients with a narrow pelvis.

Congenital Dislocation of the Hip.—Dr. S von Rosen of the Malmö General Hospital (*Nordisk Medicin*, Jan. 15, 1959) stated that since 1952 every baby has been tested shortly after birth by the Ortolani snap sign, a sensation evoked at the hip by a manipulative movement. By 1956 he was able to report on eight babies with 14 snapping hips. Roentgenograms showed upward displacement of the femur, indicative of dislocation, for which various forms of postural treatment were prescribed. In only two of these cases was it necessary to put the infant in a plaster cast for a brief period. In the other cases only ambulant treatment was required. In every case treatment was completed and the child could begin to walk when about a year old. Follow-up roentgenographic control showed normal or nearly normal development of the hips. Since 1956 six more cases have been discovered in this way and given appropriate treatment. As no other case of congenital dislocation of the hip has been discovered in Malmö during the period under review, it may be claimed that the above-mentioned procedure has proved effective in detecting this condition at birth. Improved x-ray technique with regard to both diagnosis and subsequent supervision has enabled von Rosen to shorten the fixation period.

Sympathectomy for Obliterative Arteritis.—Between 1930 and 1955 sympathectomy for obliterative arteritis was performed on 104 patients (88 men and 16 women) at the Serafimer Hospital in Stockholm. Dr. A. Kovamees (*Nordisk Medicin*, Jan. 22, 1959) made a follow-up study of these patients. Their average age at the time of operation was 53 years. The operation was undertaken to relieve intermittent claudication, pains and cramps at night, gangrene, or a sense of coldness in the limbs provoked by arteriosclerosis or diabetes. At first the operation was transabdominal but later on it was performed extraperitoneally. The operation was performed in two stages when it had to be bilateral. No deaths were attributable to the operation. Only four patients could not be traced. Of the rest 30 had died before the follow-up, which showed that for the most part even elderly patients had tolerated the operation well. Lasting improvement of claudication by itself or in combination with pain was most marked when it was associated with an efficient collateral circulation which should be a prerequisite for the operation in such patients.

Care of the Insane.—Reports of the proceedings of the Swedish Parliament give a good insight into what is happening in the country's state-owned mental hospitals. With more beds and a more rapid turnover of patients reflecting the success of modern methods of treatment, the number of admissions has risen from about 8,000 in 1950 to over 13,000 in 1957. There are now more acute cases and fewer chronic cases, with a steadily dwindling incidence during the last decades in the number of patients with schizophrenia and manic-depressive psychosis and a rise in the number of those with reactive psychosis, neurosis, psychopathy, alcoholic hallucinosis, and similar ailments. In the past many of those with acute conditions were not admitted to any mental hospital for such reasons as the deterrent effect of long waiting lists.

Willingness on the part of the patient to seek treatment in a mental hospital has increased. In 1940 barely 37% of the admissions were at the patient's request, whereas the corresponding figure for 1956 was 48%. Senile psychoses, so difficult to treat and so apt to be of long standing, continue to require from 20 to 25% of the mental hospital beds. Over 50% of them are still required for chronic conditions such as schizophrenia, but the outlook for them has improved, thanks to new methods of treatment sometimes helpful even in cases of long standing; but, although modern methods may have speeded up the turnover, the successes thus achieved have often been costly. The growing flood of acute cases now requires a complicated and costly set-up for both diagnosis and treatment, whether in the form of chemical laboratories or in the training of physicians in modern methods of psychological testing.

Functional Heart Diseases.—Since 1948 the Kristianstad Army Hospital has included a special department for dealing with functional heart diseases. Dr. G. Trönnberg (*Svenska Läkartidningen*, Feb. 6, 1959) reported a follow-up study of 164 young men who in earlier years had had a functional heart disease. These disturbances manifested themselves by dyspnea, palpitation, a precordial stabbing pain on exertion or even at rest, lassitude, or anxiety. Among the 145 who answered the questionnaire sent them were 41 who came to the hospital for reexamination. This showed that 16 had become subjectively free of symptoms. The objective picture was practically unchanged, although on the whole there had been some reduction of the blood pressure. The family histories indicated heredity as a potent influence in the genesis of the cardiac symptoms. Trönnberg urged his colleagues not to spoil such patients by prescribing tonics and the like.

Tularemia.—Between 1931 and 1956 tularemia was reported in 814 human patients. Of these 85% came from one county where the disease is evidently endemic. The remaining 15% were from all over the country, but several of them came from an area adjoining the county in question. Here about 11% of the population showed a positive reaction to specific intracutaneous tests, so it is likely that in such an endemic area the disease occurs in an asymptomatic form. During 1952 and 1953 a lookout for this disease was kept at the bacteriological department of the General Hospital in Malmö by submitting serums received for the Widal test to routine examinations for tularemia agglutinins. They were never found, but in the summer of 1958 six patients (all women) with tularemia were admitted to this hospital. Dr. S. E. Björkman and coworkers (*Svenska Lakärtidningen*, Jan. 30, 1959) stated that suspicion of tularemia was raised by the combination of recurrent attacks of fever, pain in the muscles, and a universal erythema. The diagnosis was confirmed by a high agglutination titer. Four of the six patients presented a general rash or scattered hemorrhagic patches. In some the location of the rash suggested that stinging insects may have conveyed the infection from some animal host.

UNITED KINGDOM

Abortion on Television.—The subject of abortion was discussed on the British Broadcasting Corporation's television station by a psychiatrist, a gynecologist, and a forensic pathologist, all of whom were anonymous. Two girls, with their backs to the screen, opened the program with accounts of operations they had undergone at the hands of illegal abortionists. These operations were illustrated with

anatomic diagrams and a close-up of a 3-month-old human fetus, which was shown to stress the point that at this period a miniature human being with a right to live is in existence. The pathologist presented the law on abortion. He told viewers that even when performed legally, with genuine medical indications, abortion could be dangerous and result in lifelong disability. The high incidence of criminal abortion in Britain (between 5,000 and 6,000 reported annually) and the septic conditions under which most abortions are performed were pointed out. The view was put forward that there was some benefit in legalizing abortion after rape, incest, rubella in early pregnancy, and in cases where the mother threatens suicide. The psychiatrist, however, disagreed with the last mentioned. This was an honest attempt on the part of the BBC to expose abortion as a major social evil. The program was mildly criticized by the *British Medical Journal*, which considered that the introduction was overdramatized and that a description of the complications of abortion and rubella in early pregnancy might alarm some of the viewers personally confronted with these problems, but the journal's comments were on the whole favorable.

Epstein's Brain.—Sir Jacob Epstein, the famous sculptor, made a bronze bust of Sir Russell Brain, former president of the Royal College of Physicians. The bust, presented by fellows of the college, was unveiled in the library after a dinner attended by Epstein, Brain, and the fellows. In a humorous speech Brain said "I am the speaking likeness of a bust by Epstein."

Forgotten Swab in the Abdomen.—In June, 1958, a woman was awarded $7,850 damages against a surgeon and a hospital authority for leaving a swab behind after an abdominal operation. The operation, which was an emergency procedure for repair of a ruptured uterus, was attended by excessive bleeding for which a large number of packs and swabs were used. It was estimated that 3.0 to 3.5 liters of blood were removed from the abdominal cavity. One of the swabs was inadvertently left in the abdomen. At a subsequent operation for intestinal obstruction the retained swab was found to be the cause. The judge held that the surgeon was negligent in not counting the swabs correctly and in leaving one in the patient's abdominal cavity. The case was taken to the court of appeal, where the judgment against the surgeon was reversed. He was exonerated from negligence and was in fact praised for saving the patient's life. It was held that without his speedy intervention the patient would have died from hemorrhage and that at the time the patient's condition was such that an exploration of the abdomen to look for swabs might have been fatal. The court, however, dismissed the appeal of the hospital authority, although it reduced the damages from $7,850 to $2,100. It held that there had been negligence in failing to count the swabs correctly and that the hospital was ultimately responsible for this. Operating room routine, it was argued, was designed to deal as efficiently with emergency operations as with planned operations.

Treatment of Cancer by Irradiation and Infusion of Stored Marrow.—The inevitable result of high-dosage irradiation for the treatment of cancer is bone marrow damage. This, and the unpleasant constitutional effects on the patient, has prevented the full use of radiation therapy in the treatment of metastatic tumors. Newton and co-workers described the use of stored autogenous bone marrow to combat the hematopoietic damage caused by irradiation in cancer patients (*Brit. M. J.* 1:531, 1959). The entire thorax of two selected patients with multiple pulmonary metastases was treated by means of the 2 Mv. Van de Graaff generator, delivering a dose of 3,000 r in two weeks. Two days before, during, and after irradiation the patients were given 20 mg. of prednisone and 100 mg. of vitamin K daily and 4 mg. of perphenazine three times a day. Before irradiation, with the patient under local anesthesia, bone marrow was aspirated from both iliac crests and the sternum and stored aseptically after dilution at —79 C. The volume of marrow obtained was 30 to 60 ml., containing 0.5 to 1.5 by 10^9 red blood cells. At the completion of the course of irradiation the bone marrow was thawed and injected intravenously. Within two to four weeks there was evidence of marrow regeneration in both patients. They tolerated the radiation well and experienced no immediate untoward side-effects directly attributable to it. The first patient had severe dyspnea and respiratory symptoms, but this was almost certainly due to the progress of the pulmonary metastases. The results showed that the entire thorax can be irradiated to 3,000 r in two weeks with no constitutional disturbance.

Immunization Against Helminthic Infection.—Although much experimental work has been published, the control of heminthic infection by vaccines has not hitherto been possible. A group of workers at the Glasgow Veterinary School has solved the problem of the helminthic infection of young cattle, called "husk," by administering a vaccine made from larvae attenuated by irradiation (*Proc. Roy. Soc. Med.* 51:743, 1958). The causative organism settles in the lung of calves, in which it causes high morbidity and mortality. Recovered cattle have a strong immunity to reinfection. The Glasgow workers found that some degree of immunity was afforded by intramuscular injections of whole worm vaccine, but that an oral vaccine of living but attenuated infective larvae was even more effective in preventing infection. The essential part of the technique is attenuation of the larvae by

irradiation with roentgen rays before administration as a vaccine. The attenuated larvae migrate from the intestine to the lungs through the mesenteric lymph nodes, but here they die after provoking the necessary antigenic action. This technique has been explored with success in other helminthic infections of dogs and cattle, such as hookworm, cysticercosis, and nematodiasis.

Complications of Steroid Therapy.—Three cases of intestinal perforation after the administration of steroids to patients with rheumatoid arthritis were reported by Parker and Thomas (*Brit. M. J.* 1:540, 1959). One patient, who was treated with 30 mg. of prednisolone daily and then 150 mg. of cortisone daily, developed severe abdominal pain. Laparotomy revealed a recent 4-cm. perforation of the sigmoid colon. The perforation was repaired but the patient died from peritonitis. Another patient, under treatment with cortisone, died from the same condition after perforation of the cecum. The duodenum was perforated in the third patient, who was under treatment with cortisone. It was repaired but the patient died the following day. At autopsy the three patients were found to have widespread arteritis with fibrinoid necrosis. These patients had had no preexisting gastrointestinal disease. It was concluded that the intestinal perforation and arteritis were abnormal reactions to the cortisone.

Frozen Eye Bank.—Dr. B. Rycroft stated that eyes may soon be preserved almost indefinitely by deep-freeze storage. Corneal grafts have been thus preserved for many weeks, compared with one week's storage by older methods. The difficulty of corneal grafting at the moment is not only obtaining enough eyes but getting fresh material. Long-term preservation of eyes in an eye bank would help to solve this problem. Successful corneal grafting operations have risen from 10% 20 years ago to 60% today. In Britain the supply of grafting material has markedly increased since the passing of the Corneal Grafting Act of 1952, which awakened the public conscience to the needs of the blind. At the Corneo-Plastic Unit, East Grinstead, the number of eyes received now is six times what it was before the passing of the act. A mobile team is present at the unit ready to collect eyes from recently deceased persons. If deep-freeze storage proves successful, an eye bank could be built so that eyes for corneal grafting would always be available for the whole country. Rycroft said that the bequest of eyes after death is a direct contribution to the relief of blindness in this country. It is a gift of the highest order of humanity which anyone with normal eyes can easily make.

Fetal Tissue Bank.—Grafts of living cells exchanged between unrelated members of a species are destroyed after a short interval by an immune response of the host's lymphoreticular system—the so-called homograft reaction. Exceptions to this occur where the graft is "insulated," as in the cornea, or where the host's immune system is ineffective owing to immaturity, as in the fetus. Kay and Constandoulakis discussed the possibility of using fetal hematopoietic cells for transplantation after massive irradiation, either accidentally induced or from high-dosage radiotherapy (*Brit. M. J.* 1:575, 1959). The supply of human fetal tissue is severely limited, as during the first three months of pregnancy the fetus is small and seldom obtainable in a sterile and intact form. In the last three months, as the fetus is legally alive, the parents' consent must be obtained for disposal. Fetuses are also obtained as a result of terminations of pregnancy between 12 and 18 weeks. Twelve hours after delivery the cells of the fetus are no longer viable at room temperature, although if kept at 4 C cell death is appreciably delayed.

The authors organized a 24-hour service with the help of gynecologists in many London hospitals. The liver is the main source of fetal hematopoietic cells. No attempt was made to use spleen or bone marrow. The liver was dissected under sterile conditions and reduced to a cell suspension by pressing through a wire mesh, removing stroma, and breaking the tissue up into individual cells, which were cultured anaerobically and aerobically and stored at 4 C for 12 to 24 hours or at —79 C for longer periods. Short-term culture of a cell suspension can be made at this stage. Cells are preserved at —79 C for months or years. Using the technique of autoradiography the authors showed that desoxyribonucleic acid synthesis continues after freezing and thawing in 15% glycerol serum, but they did not know what proportion of stem cells survived. It costs less than $280 per year to store 5 liters of fetal tissue suspension, or about 3 by 10^{13} cells, by means of dry ice. Suspensions of these thawed cells can be given intravenously. By virtue of some extraordinary homing instinct these cells find their way to the appropriate site in the body, where they settle and multiply.

New Penicillin.—An important development in the antibiotic field was made by Batchelor and coworkers, of the microbiological unit of the Beecham Research Laboratories (*Nature* 183:257, 1959). They isolated from penicillin cultures 6-aminopenicillanic acid, from which a number of new penicillins may be obtained. It is hoped thus to produce penicillin O (allylmercapto-methyl penicillin) and cephalosporin N (α-amino-adipic penicillin), which do not cause reactions in penicillin-sensitive subjects. A new approach to the problem of penicillin resistance, particularly staphylococcic, is now a possibility. It is hoped that the new penicillin derivatives may prove active against such resistant organisms. Means may be found for increasing the activity of penicillin-type compounds against

gram-negative bacteria. Some of the new penicillins are being tested against the organisms of whooping cough, scarlet fever, diphtheria, gas gangrene, tetanus, typhoid, meningitis, leprosy, and respiratory infections.

New Tranquilizer.—Stelazine (trifluoperazine hydrochloride), a fluorinated derivative of prochlorperazine, is a new tranquilizer. Macdonald and Watts used it to treat 50 patients with acute and chronic paranoid schizophrenia (*Brit. M. J.* 1:549, 1959). The dose given was 5 mg. daily for the first three days, thereafter increasing by 5 mg. daily at three-day intervals until side-effects were produced or until a satisfactory therapeutic result had been obtained. When symptoms had been controlled the dosage was reduced to a maintenance level on which the patients were free from side-effects and at which the therapeutic effect seemed maximal. The maximum dose was 45 mg. daily and the average maintenance dose was about 22.5 mg. daily. Trifluoperazine was given to 30 male chronic paranoid schizophrenics who had been hospitalized for at least two years, and to 20, admitted during the first attack of less than six months' duration, who had not had any previous treatment. The results were judged on the basis of the patients' capacity for adjustment to normal social surroundings. Of the 30 chronic cases 21 showed improvement ranging from suitable adjustment to life in the hospital community (12) to discharge from hospital to full employment (5). The results in the early cases were gratifying. Of the 20 acute cases 14 were able to return to full employment and 6 were well-adjusted socially within the hospital community. Trifluoperazine should prove a valuable addition to the drugs available for the treatment of schizophrenia.

Physiotherapy in Arthritis.—The value of physiotherapy in patients with arthritis was assessed by Hamilton and co-workers (*Brit. M. J.* 1:542, 1959). A trial was designed to study the effect of short-wave diathermy, infrared radiation, faradic stimulation, and paraffin wax baths on functional improvement in patients with rheumatoid arthritis or degenerative joint disease involving the hands or knees. These joints were chosen because they are the easiest in which to assess function accurately. Sixty-two patients were treated for a month with each form of therapy selected at random and the results compared with a period in which no physiotherapy was given. In addition, all patients were given analgesics and splinting as required, with active exercises after the treatment. Range of movement, power of extension of the joints, and the time taken to walk up and down standard stairs and over a measured distance were calculated for each patient before and after each treatment. No significant difference was found among any of the four treatments, nor was there evidence that any of the forms of physiotherapy gave significantly better results than no treatment, other than that with simple exercises, splinting, and analgesics. The authors concluded that the most useful physiotherapeutic measures for arthritics are those maintaining muscle power and joint movement by active exercise, good posture, and coordination of movement.

Fetal Blood Cells in Maternal Circulation.—It has recently been shown that the hemoglobin of adult red blood cells in a fixed smear can be eluted by an acid phosphate buffer, whereas the hemoglobin of fetal blood cells cannot. Using this test Zipursky and co-workers showed the presence of fetal blood cells in the blood of women just after delivery (*Lancet* 1:451, 1959). Smears of in vitro mixtures of fetal and adult blood were scanned for two minutes under the microscope. The number of fetal red blood cells counted varied from 2 in a dilution of 1:25,000 to 21 in a dilution of 1:1,000. When three adults were given 3.5 and 15 ml. of compatible placental blood intravenously, the fetal cells were demonstrated in the expected concentration in their blood. No fetal cells were found in male and nonpregnant female blood donors. The blood of 42 mothers, selected at random, and recently delivered, was examined on the second and sixth day post partum. In a two-minute scanning 1 to 16 fetal red blood cells were seen in 21% of the films. A count of 16 corresponds to 2 ml. of fetal blood in the maternal circulation. These observations suggest that the placental passage of fetal blood into the maternal circulation is common.

Atherosclerosis in Jamaicans.—Many workers have concluded that populations living on high-calorie high-fat diets have a higher mean serum cholesterol level and are more prone to develop ischemic heart disease than those living on simpler diets. Much of the evidence for this is circumstantial. Robertson recorded the incidence of atherosclerosis of the aorta at 500 autopsies in Jamaicans and has compared it with that in published series elsewhere in the world (*Lancet* 1:444, 1959). The population of the area studied was partly urban and partly rural, mostly Negro, with a few East Indian, Chinese, or Caucasian subjects. The predominantly Negro population in Jamaica was found to develop a degree of aortic atherosclerosis similar to that of a mixed population studied in New Orleans. The incidence of atherosclerosis runs parallel to that of ischemic heart disease in New Orleans, but not in Jamaica, where the incidence of myocardial infarction is much lower. Robertson therefore concluded that, since there is no constant relation between the incidence of atherosclerosis and that of coronary thrombosis, they are unlikely to have the same cause. He also stated that cerebral thrombosis, phlebothrombosis, and pulmonary embolism are comparatively uncommon in Jamaicans.

CORRESPONDENCE

CIRCULATING BLOOD VOLUME CHANGES

To the Editor:—It was distressing to read the article "Circulating Blood Volume Changes Incident to Major Orthopedic Surgery," by Powers and Hensley, in THE JOURNAL, Feb. 7, page 545. The major assumptions made in the article are that (1) any fluid administered into the vascular space remains there as is, in total; (2) iodinated albumin remains in the space to be measured, without leaving the circulation, for about 10 minutes; (3) no compensatory mechanisms are in progress during the surgical and anesthetic procedure, as well as during the mixing period; and (4) technically, a ±6% accuracy is obtainable in vivo.

None of these assumptions hold true when an intravascular volume is measured with plasma-bound elements. Phenomena of hemodilution and loss of fluid from the intravascular space are constantly in operation and are reflected in plasma volume changes. Whole blood and salt or glucose infusion have varying effects on the total volume (Thistlethwaite and others, *Surg. Gynec. & Obst.* 105:34-38 [July] 1957; Albert and others, *Anesth. & Analg.* 36:54-61 [Sept.-Oct.] 1957; Albert and others, United States Atomic Energy Commission Technical Information Service, no. AECU-3614 [March] 1957). Iodinated serum albumin leaves the intravascular space at a variable rate dependent on many factors (Gitlin, *Ann. New York Acad. Sc.* 70:122-136 [Aug. 30] 1957). Technically, to obtain a ±6% in vitro with iodinated albumin is very difficult due to the adherent properties of Risa to glassware (Reeve, *Ann. New York Acad. Sc.* 70:137-149 [Aug. 30] 1957).

The only correct method for measuring blood loss is measurement of total circulating red cell volume with red cells tagged with Cr^{51}. The technique is simple with no technical errors involved. Grave errors in judgment and measurement can be made by just measuring a total volume without estimating the cellular element, which is the only reliable method.

I do not contest the fact that considerable amounts of blood are lost during orthopedic surgery—far more than is estimated clinically; but I cannot agree with the method used and am sure that with proper measurements the facts and results would still be more striking. An additional measurement made 24 hours postoperatively would show the considerable blood loss that occurs from oozing.

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To the Editor:—We believe that the validity of blood volume determinations with use of radioiodinated serum albumin is well established provided proper precautions are taken to reduce technical error. In fact, Hlad and Tanz (*J. Lab. & Clin. Med.* 52:289-298 [Aug.] 1958) reported a standard error of ±2% in vivo! That compensatory mechanisms are at work during anesthesia and operation is not questioned. Insofar as they do influence blood volume, it appears to be obvious that any blood volume determination, regardless of method, must reflect the changes they occur. Otherwise, the blood volume determinations would be without value.

The statement that the use of tagged cells is the only correct method, simple and without technical error, we believe, is open to debate. Adherence of chromium to glass has been reported (Small and Verloop, *J. Lab. & Clin. Med.* 47:255-260 [Feb.] 1956). Irregular mixing of radiochromate-labeled erythrocytes in the spleen has also been reported (Kraintz and others, abstracted, *Fed. Proc.* 17:89 [March] 1958). Pooling of erythrocytes probably occurs during operation. All of these factors can influence the accuracy of the method.

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FALL-OUT AND LEUKEMIA

To the Editor:—In the United Kingdom foreign letter in THE JOURNAL, March 14, page 1234, is a note on fall-out and leukemia. The statement is made that I^{131} has never been linked with leukemia. The *New England Journal of Medicine* (260:76-77 [Jan. 8] 1959) contains an account of the sixth reported case of leukemia after use of I^{131} for hyperthyroidism. One of the six reports was in THE JOURNAL (165:1558-1559 [Nov. 23] 1957).

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FALSE-POSITIVE REACTION FOR ACETONURIA

To the Editor:—While testing, with phenolsulfonphthalein (PSP), the renal function of a patient with well-regulated diabetes mellitus, a strongly positive reaction for acetonuria was noted. This false-positive reaction was noted with the conventional test for acetone, using sodium nitroprusside, as well as with Acetest tablets (Ames Co.) and acetone test powder (Denco). These color reactions

could be reproduced with PSP diluted with water and are undoubtedly due to the fact that all three tests for acetone take place at an alkaline pH. The color produced by PSP is not exactly identical with that produced by acetone but is sufficiently similar to provide a source of error. The false-positive test result for acetone can readily be distinguished from true acetonuria by the failure of PSP to evaporate on boiling. The color could also be distinguished by spectroscopy, but this method of examination is not generally available. A positive ferric chloride test result for diacetic acid is not given by PSP.

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MISCELLANY

PHYSICIAN WHO SERVED ON THE U. S. SUPREME COURT

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Probably few physicians today are aware that their profession once contributed an eminent justice to the Supreme Court of the United States. He was Dr. Samuel Freeman Miller, a gentleman from Kentucky who was appointed to the Supreme Court in 1862 by President Lincoln. He served with distinction as an associate justice of this court for the next 28 years and on several occasions was considered for promotion to chief justice, although this honor went in 1864 to Salmon P. Chase, in 1874 to Morrison R. Waite, and in 1888 to Melville W. Fuller.

Dr. Miller was a lawyer as well as a physician, but until he studied medicine, and later law, he had had no formal education whatever. When he sat on the bench, however, he was regarded as an able and forceful exponent of the law, if not a scholarly one.

Born at Richmond, in the blue grass region of Kentucky, in 1816, Dr. Miller was only 20 years old when he entered the medical department of Transylvania University at Lexington. There he attended lectures for one year, leaving to teach school for a few months and returning to the medical department late in 1837 for less than six months, at which time he passed the necessary examinations and was awarded the degree of doctor of medicine early in 1838. With this sketchy foundation in medicine, in contrast to the eight or more years of college, medical school, internship, and residency required of modern American physicians, Dr. Miller set up in general practice in the mountain community of Barbourville, Ky.

Here he practiced medicine for the next 12 years, bleeding and purging his patients in accordance with the ideas of the times. He also became interested in a debating society, participated in politics as an antislavery Whig, and was appointed a local justice of the peace. These activities stimulated an interest in law. In those days the budding attorney, like many an aspiring medical student, usually served an apprenticeship with an older, established practitioner; but some, like Lincoln himself, merely read profusely in the commentaries of Blackstone, Story, and Kent and other available legal texts. Miller read so well that he was admitted to the bar in 1847.

Three years later he moved to Keokuk, Iowa, where he engaged in the practice of law. He also participated heartily in the activities of the newly formed Republican party. He was an ardent supporter of Abraham Lincoln, who in 1862 nominated Miller to the Supreme Court, an appointment which received the unanimous approval of the Senate. When Miller took his seat the Chief Justice was Roger B. Taney of Maryland, who had been appointed to this office in 1836 by President Jackson after the death of the great John Marshall, who had served for 34 years. Taney, incidentally, was a Roman Catholic, one of the first of his faith to hold this high office in the Republic.

During his nearly three decades on the bench of the Supreme Court, Mr. Justice Miller participated in some 5,000 cases and delivered the opinions for the court in 600 of them. One of these opinions, handed down in 1873 in the Slaughter House Cases (*16 Wall 36*), has a certain medical significance, since it held that an action by the state of Louisiana in granting a monopoly for the slaughtering of animals was a valid exercise of police power in the interests of the public health and not in contravention of the rights granted by the federal constitution.

Mr. Justice Miller, M.D., has been described as a tall, massive man, inclined to be domineering. Although self-educated, he was extremely well versed in the law. He died in 1890 at the age of 74. Although by no means the only physician who ever studied law and made a career of it, he was the only physician to sit on the Supreme Court of the United States, which in the course of 170 years has had 94 justices.

MEDICAL FILM REVIEWS

Portal Decompression: 16 mm., color, sound, showing time 29 minutes. Prepared by Charles G. Child, M.D., Boston. Produced in 1958 by Sturgis Grant Productions, New York, for and procurable on loan from E.R. Squibb and Sons, 745 Fifth Ave., New York 22.

This film is divided into two sections. In the first part animated diagrams depict the anatomy and physiology of the hepatic circulation and explain the etiological factors responsible for portal hypertension in terms of the clinical picture presented. In the second, a patient is introduced for whom portal decompression is indicated, and the surgical procedure for an end-to-side portacaval shunt is shown. The film demonstrates the value of audiovisual educational technique when proper coordination exists between the surgical team, the illustrator, and the photographic crew. The subject is presented in a style which is interesting and easy to understand. At all times the viewer knows what is being discussed or what is being done. An end-to-side portacaval shunt is demonstrated in a rather muscular and obese patient. This is a difficult photographic exposure to obtain; however, the anastomosis can be seen clearly. The emphasis placed on the importance of dilated lymph vessels, which may be injured during the course of dissection and thereby add to the morbidity or mortality, is particularly commendable. The author is also to be commended for the use of the term "esophagogastric varicosities" rather than merely esophageal varices. This film can be recommended to surgeons, medical students, and nurses.

Intracellular Recording in the Mammalian Heart: 16 mm., color, sound, showing time 21 minutes. Prepared by Theodore C. West, Ph.D., University of Washington. Produced in 1958 under a grant from the National Heart Institute, National Institutes of Health. Procurable on rental ($3.75) or purchase ($140.00) from The Film Center, University of Washington, Seattle 5.

This film presents a concise demonstration of the recording of membrane potentials of the various cardiac cells, in both the isolated atrium of the rabbit's heart and the dog's heart in situ. It acquaints the viewer briefly with the method of recording the potentials of individual cells with the floating glass electrode. The sequence showing depolarization and repolarization of cells in the sinoauricular node, in the atrium, and in the ventricle and the relation of the muscle to contraction are very well demonstrated. Changes induced by drugs (epinephrine and quinidine) and by variation of blood temperature are also shown. The photography and narration are excellent. The film has great teaching value, and it should be most welcome to all students of cardiac physiology and pharmacology.

Dynamics of Phagocytosis: The Interaction Between Group A Streptococci and Human Neutrophils in Vitro: 16 mm., black and white, sound, showing time 37 minutes. Prepared in 1958 by Armine T. Wilson, M.D., Wilmington, Del. Procurable on loan from Pfizer Laboratories, 630 Flushing Ave., Brooklyn 6, N. Y.

This film shows dynamically the process of phagocytosis, including chemotaxis, contact, ingestion, egestion, and leukotoxicity; and it depicts the events that occur when living streptococci and leukocytes interact in vitro. The phenomena of hemolysis, chemotaxis, and virulence are elucidated in relation to phagocytosis. The behavior of leukocytes and monocytes is shown. These and other interesting manifestations in the natural history of phagocytes are clearly and instructively illustrated. The film is well done and can be recommended for showing to medical students, biology students, physicians, and all interested in problems of immunity and susceptibility to disease.

Thursday's Child: 16 mm., color, sound, showing time 23 minutes. Produced in 1958 by and procurable on loan from Children's Medical Center, 4900 S. Lewis, Tulsa, Okla.

This film presents the diverse medical therapy programs available in the Children's Medical Center, including psychiatric service; child guidance clinic; school for the mentally retarded; training program for physicians, psychologists, and other medical personnel; and a 62-bed children's hospital providing a full program of rehabilitation for all types of children's disabilities. With the aid of a narrator and background music the viewer "tours" the medical center. The film deals with the story of the center's daily activities in caring for numerous physically and mentally disabled children. While it does not attempt to portray or teach any specific medical techniques, it is nevertheless interesting and should be of considerable help in stimulating the interest of the public and the medical profession in such activities.

Varicose Veins: 16 mm., color, sound, showing time 7 minutes. Produced in 1958 by Churchill Wexler Film Productions for and procurable on loan or purchase from the American Heart Association, 267 W. 25th St., New York 1.

The conditions leading to the development of varicose veins and methods of prevention and treatment are discussed in this film. Animation is used to illustrate the function of the blood vessels and valves related to understanding the problems of varicose veins. The onset and effects of relaxation of the vessels eventuating in varicose veins are depicted, and the anatomy of the veins is shown. The film points up the preventive measures, as well as what can be done when the condition develops. It is scientifically accurate and is highly recommended for adult audiences and also for family-living classes in high school and college.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Duodenal Ulcer Amongst Africans in Nairobi. Ashfaq Alam Khan. East African M. J. 35:679-684 (Dec.) 1958 [Nairobi].

The series of 28 patients with duodenal ulcer presented were admitted to the King George VI Hospital in Nairobi, Kenya, from August, 1957, to May, 1958. There were 20 males and 8 females. The criteria for diagnosis were: (1) a characteristic history; (2) a history of hematemesis or melena; and (3) the roentgenologic demonstration of an ulcer crater. The last factor was an essential prerequisite for inclusion in this study. The annual report published by the Kenya Medical Department shows the number of cases of duodenal ulcer in a rising curve, with a steep rise in 1956; similarly the figures for the King George VI Hospital show an upward trend. No particular liability or proneness to develop duodenal ulcer was observed in any tribe, nor was any tribe immune from it. All but 3 of the patients were between 18 and 40 years of age. All social groups were represented, and educational standards had no bearing on the incidence.

A dietary regimen, continued for 4 weeks, produced freedom from pain in 21 of the patients. All 10 who were reexamined 6 months later showed a healed ulcer on roentgenologic examination. Two others experienced relapses and had to be readmitted. One required gastroenterostomy. Four showed no improvement and refused operation. The author feels that medical treatment is adequate for the type of duodenal ulcer found in Africans, since the ulcer is generally small. One should resist the temptation to operate and try to persevere with repeated courses of medical treatment.

When people from the reserves come into the cities and take to a new mode of life, they are subjected to all the stresses and strains of the modern world. This may give rise to all sorts of anxiety states. In Africa, just as in any other part of the world, there are certain individuals who are ulcer prone, or have a large number of acid secreting glands in the stomach. The African reacts to the stress and strain of the pace of modern life in the same fashion as any other individual, and so is equally liable to get any of the stress diseases, of which duodenal ulcer is one.

The Role of Thoracotomy in the Differential Diagnosis of Pleural Effusion. J. M. Schless, H. N. Harrison and J. A. Wier. Ann. Int. Med. 50:11-33 (Jan.) 1959 [Lancaster, Pa.].

In an attempt to establish better criteria for the differential diagnosis of pleural effusion, the authors report on 63 patients with pleural disease who underwent open thoracotomy at the Fitzsimons Army Hospital in Denver between 1953 and 1956. The pleural involvement in all these patients either was due to tuberculosis or at some point in the course of the disease was seriously considered to be tuberculous pleuritis, or this condition could not be clinically excluded. The final diagnosis in 38 of the 63 patients was tuberculosis, and the remaining 25 patients were given a final diagnosis of nontuberculous pleuritis. The indications for thoracotomy were primarily diagnostic in 17 patients; in 14 patients the indications were both diagnostic and therapeutic; and in the remaining 32 patients thoracotomy was primarily a therapeutic procedure. Of the 63 patients, decortication was performed on 57, and 6 underwent open pleural biopsy in the course of a full exploratory thoracotomy. Pulmonary tissue was obtained by biopsy from 30 of the 63 patients.

All patients with the final diagnosis of tuberculosis had positive results from tuberculin tests. All patients with negative results from tuberculin tests were in the group with a final diagnosis of nontuberculous pleuritis. It is felt that a negative tuberculin test, done with properly prepared solutions and repeated 6 to 8 weeks after the onset of the effusion, effectively excludes tuberculosis as the cause of a given pleural effusion. However, positive results from tuberculin tests prove nothing as far as establishment of a diagnosis of tuberculosis is concerned, other than the fact that tuberculosis must be considered a possibility. The pleural fluid did not show consistent physical, chemical, or morphologic differences that could be relied upon to differentiate tuberculous from nontuberculous effusions. Only 7 (21%) of the 38 patients with a final diagnosis of tuberculosis had positive bacteriological findings on the pleural fluid aspirate. The

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incidence of positive sputum and/or gastric aspirates (in only 14 [40%] of the 38 patients) was too low to be of differential diagnostic value in the negative sense.

Morphologic pleural changes established the presumptive diagnosis in 32 of the 38 patients. In 3 additional patients the diagnosis was established by the morphology of lesions discovered in the lung at the time of thoracotomy. In these 3 patients the diagnosis would never have been established had not full open thoracotomy with careful palpation of the lung been done. Thus, morphologic changes in the pleura and/or the lung established the diagnosis in 35 of the 38 patients. Morphologic findings in tissue obtained at open thoracotomy were, therefore, at least 92% reliable in this series in differentiating tuberculous from nontuberculous pleural effusions. Morphologic findings were unaffected even by prolonged chemotherapy in practically all patients, but the chances of bacteriological confirmation proved to be inversely proportional to the duration of preoperative chemotherapy. The specific drug regimens used did not seem to be important.

Follow-up information of from 6 months to 3½ years after discharge was available in 45 patients (71%). None of the patients with tuberculosis had relapsed, and in none of the patients who were cleared as having nontuberculous pleuritis had any evidence of tuberculosis developed since time of discharge. There seems to be a strong indication for a controlled study utilizing exploratory thoracotomy in pleural effusions of dubious causation. Except for a short period of preoperative drug coverage in all patients, antituberculous chemotherapy should be withheld in all patients who do not show morphologic or bacteriological changes compatible with tuberculosis. A long-term follow-up study on such a series of patients would seem to be of great value.

Whipple's Disease: Report of Four Cases, Including Two in Brothers, with Observations on Pathologic Physiology, Diagnosis, and Treatment. J. B. Gross, E. E. Wollaeger, W. G. Sauer and others. Gastroenterology 36:65-93 (Jan.) 1959 [Baltimore].

The authors report on 2 brothers, aged 62 and 63 years, and on 2 additional men, aged 44 and 50 years, with intestinal lipodystrophy (Whipple's disease), in all of whom the clinical and pathological pictures were typical. The cases of the 2 brothers constitute the second recorded occurrence of intestinal lipodystrophy in siblings. Some of the relatives of the 2 brothers had mental illness and diabetes mellitus, and the parents of the 4th patient also had diabetes mellitus and a "nervous condition." These findings suggest that diabetes mellitus and mental disease may be unusually prevalent among the relatives of persons with intestinal lipodystrophy. The pathological and clinical features of the 4 patients and of those reported on by other workers convinced the authors that intestinal lipodystrophy should be suspected in middle-aged white men with a chronic, wasting, steatorrheal diarrhea associated with antecedent migratory polyarthralgia. [To date the disease appears to have affected the white race exclusively, almost always men, and usually those of middle age.] Many patients had chronic cough, hives, chills and fever, ill-defined abdominal distress, and marked loss of weight. The patients usually appeared weak and wasted. Hyperpigmentation and hypotension were found in most of them, and peripheral lymphadenopathy was a common observation. Many patients exhibited an abdominal mass. The characteristic hematological findings were hypochromic anemia, increased erythrocyte sedimentation rate, and absence of macrocytosis. The concentration of mucoprotein in the serum was characteristically increased. Roentgenographically there was usually a deficiency pattern of the small intestine, and occasionally roentgenograms of the joints and spinal column revealed changes suggestive of rheumatoid arthritis.

Microscopic examination of the peripheral lymph nodes frequently revealed the presence of noncaseating granulomas suggestive of sarcoidosis. These nests of macrophages take the periodic acid–Schiff stain. Although the microscopic picture is not by itself specific, when it occurs in a patient with the characteristic clinical picture of intestinal lipodystrophy, the combination should serve to make one suspect more strongly this disease. The absolute diagnosis of intestinal lipodystrophy is a pathological one, resting on histological demonstration of macrophagocytosis of the tunica propria of the small intestine and mesenteric lymph nodes, and lipogranulomatosis of the mesenteric nodes. In the differential diagnosis of intestinal lipodystrophy clinically, one must consider sprue, adrenal cortical hypofunction (Addison's disease), Hodgkin's disease or other lymphoma, sarcoidosis, intra-abdominal malignancy, tuberculosis, regional enteritis, and chronic ulcerative colitis, as well as external pancreatic insufficiency.

The phenomenon of delayed excretion of water with regular nocturnal diuresis was observed in all 3 of the 4 patients in whom this phenomenon was tested. One of these 3 patients had a normal rate of absorption of heavy water in the fasting state. The diarrhea associated with intestinal lipodystrophy may or may not be bloody, but steatorrhea and azotorrhea are usually present, and the fecal fat and nitrogen losses may be similar to those characteristic of severe nontropical sprue and external pancreatic insufficiency.

Steroid therapy with cortisone, corticotropin (ACTH), and prednisone (Meticorten) proved disappointing in the 4 patients. The reports by other

workers suggest that such treatment has usually been variable in effect and mainly of symptomatic help. One of the 4 patients had an apparently spontaneous remission, which included complete disappearance of the marked steatorrhea and which lasted almost 4 years preceding death.

Steroid Therapy in Pulmonary Fibroses. A. G. W. Whitfield. Brit. J. Dis. Chest **53**:28-40 (Jan.) 1959 [London].

Of 35 patients with nontuberculous pulmonary fibroses and infiltrations treated with corticoids at the Queen Elizabeth Hospital in Birmingham, England, 6 had pulmonary sarcoidosis, 9 had irradiation damage of the lungs, 4 had diffuse interstitial fibrosis of the lungs (Hamman-Rich syndrome), and 16 had pulmonary infiltration occurring in collagen diseases, such as systemic lupus erythematosus (12), scleroderma (3), and polyarteritis nodosa (1). The results obtained with steroid therapy in these patients and the published reports by other workers showed that patients with pulmonary sarcoidosis in its earlier stages responded well to this therapy; it should be employed in all patients with respiratory symptoms or with progressive or persistent lung lesions. Permanent maintenance therapy is necessary to avoid relapse. Patients with irradiation damage to the lungs in the stage of pneumonitis appeared to respond to steroid therapy, and treatment for 3 months is suggested for all such patients. Patients with long-standing fibrosis did not respond, and corticoids are not considered to have any prophylactic value. The patients with the Hamman-Rich syndrome, except for one, were therapeutic failures; but since no other treatment can be offered, steroids must always be given a trial. The pleural lesions of systemic lupus erythematosus responded dramatically to steroid therapy. The interstitial pneumonitis occurring in this disease showed a less satisfactory response, but both pulmonary and pleural lesions should always be treated with corticoids. Permanent maintenance therapy is required to avoid relapse. The pulmonary lesions of scleroderma are unlikely to be improved by steroid therapy. The author's patient with pulmonary lesions associated with polyarteritis nodosa did not respond to steroid therapy, but 3 patients reported on by other workers did, and this therapy should be employed in every patient with polyarteritis nodosa.

Pulmonary Aspergillosis with Cavitation: Iodide Therapy Associated with an Unusual Electrolyte Disturbance. J. P. Utz, J. L. German, D. B. Louria and others. New England J. Med. **260**:264-268 (Feb. 5) 1959 [Boston].

The authors report on a 47-year-old man and on a 63-year-old woman with an infection due to Aspergillus niger, associated with marked cavitation and abscess formation in previously damaged lung tissue. Carcinoma of the lung in the man and repeated attacks of pneumonia in the woman were the underlying diseases which presumably provid[illegible] the appropriate environment for the superimposed fungous infection. Both patients were treated with a saturated solution of potassium iodide. The man received 30 Gm. daily for 2½ weeks, and the woman was given 24 Gm. daily for 3½ weeks; in addition, surgical drainage of the cavity was carried out in the second patient. Clearing of Aspergillus organisms from the sputum and lung tissue or abscess drainage material resulted from the treatment. Potassium iodide therapy was associated with a disturbance of the mental condition, manifested by exaggerated demands and disorientation in the woman. Hypopotassemia, with elevation of serum carbon dioxide content, and hyponatremia developed in both patients. In the woman, this bizarre electrolyte disturbance was associated with weight gain and with persistent excretion of sodium in a hypertonic urine, and these features suggest that the disturbance was due to inappropriate secretion of antidiuretic hormone, although the level of the serum electrolytes improved significantly in both patients when iodide therapy was discontinued. The woman also had hypocalcemia and hypophosphatemia for which no explanation could be given.

Pellagra in Ireland. E. A. Martin. J. Irish M. A. **44**:11-15 (Jan.) 1959 [Dublin].

Three patients with pellagra were admitted to a private psychiatric hospital in Dublin. The first patient was a 42-year-old woman who had classical pellagra, showing, in sequence, diarrhea, dermatitis, and severe mental and neurological disturbance with stomatitis. The cause was probably a deficient diet of psychogenic origin. Death appears to have been due to unrecognized recurrence. The second patient was a 63-year-old woman who had acute confusional psychosis due to dieting, vomiting, and possibly malabsorption after gastroenterostomy. The first acute disturbance followed an operation. There was no dermatitis or glossitis. Within 3 days after onset of intensive oral and intramuscular vitamin therapy, diarrhea and incontinence ceased. The patient's mental state began to improve, and she took an interest in her surroundings. Within one week all confusion had disappeared. Her general health improved, and she put on weight. Oral vitamin therapy was continued. The third patient, a 49-year-old man, presented, in sequence, mental symptoms, a rash, and diarrhea. No dietary or intestinal cause was found. Sulfaguanidine, isoniazid, and streptomycin probably precipitated an acute confusional psychosis.

Since the patients were not poor, it is suggested that pellagra might be commoner in Ireland than is generally supposed. All 3 patients had passed through general hospitals, their condition undiag-

nosed. This emphasizes that the widespread view that pellagra is seen only in mental hospitals is untrue. Pellagra may be expected to occur chiefly in the elderly person living alone, the destitute, the mentally ill, the eccentric, the alcoholic, and those with some chronic gastrointestinal disease. Pellagra is caused by a deficiency of nicotinic acid. Often there is associated deficiency of other factors of the vitamin B complex—riboflavin and pyridoxine. The richest sources of nicotinic acid are meats, liver, kidney, heart, and yeast. Whole-wheat bread and cereals are good sources, but white bread, fish, milk, eggs, fruit, and vegetables have a poor content. Pellagra may develop secondary to infection or operation which may increase the need for vitamins, loss of appetite, enforced or prescribed dieting, vomiting, malabsorption due to rapid intestinal transit or steatorrhea, and alteration in intestinal flora. The foods rich in nicotinic acid are usually excluded in peptic ulcer diets. There is evidence that alterations in intestinal flora may be of importance. Bacterial biosynthesis of nicotinic acid in the intestine may produce up to 80% of the body requirements of this substance. Succinylsulfathiazole by its sterilizing action inhibits this production. Broad-spectrum antibiotics might be expected to have an even more potent effect.

The Treatment of Moderate and Severe Pneumococcal Pneumonia with Oral Phenoxymethyl Penicillin. J. T. Reeves, J. Garfield, N. Polasky and M. Hamburger. A. M. A. Arch. Int. Med. **103**:184-188 (Feb.) 1959 [Chicago].

In this report on the oral administration of phenoxymethyl penicillin (penicillin V) in the treatment of patients with pneumococcic pneumonia at the Cincinnati General Hospital, the authors add their experience of 1956-1957 to that of 1955-1956. In general, the results obtained during the second year on 68 patients confirmed those of the first year. Whereas during the first year's investigation several dosage schedules were explored, all patients during 1956-1957 were given an oral dose of 250 mg. of phenoxymethyl penicillin on admission and every 6 hours thereafter for from 3 to 14 days. Fifty-nine patients (87% of the 68) responded within 24 hours to the oral administration of phenoxymethyl penicillin with marked clinical improvement and prompt lysis of fever. The average duration of fever was 1.8 days, and no patient remained febrile beyond the 4th day.

The oral administration of phenoxymethyl penicillin has been shown to be an effective form of therapy for moderate and severe forms of pneumococcic penumonia. Oral therapy avoids the pain of injection, the expense and effort of sterilizing needles and syringes, and the dangers of needle-borne serum hepatitis. Although phenoxymethyl penicillin is not recommended for patients critically ill or having the purulent complications of pneumonia, it may be used with safety and confidence in the great majority of patients with pneumococcic pneumonia. The optimum dosage has not been established. Although patients treated by the authors were given 250 mg. every 6 hours, equivalent to approximately 1,600,000 units, patients treated by others received the same dose at 12-hour intervals, with similar results. Because an occasional patient fails to absorb phenoxymethyl penicillin as well as most subjects, the larger dose may be a safer one.

A Review of Fifty-One Cases of Multiple Myeloma: Emphasis on Pneumonia and Other Infections as Complications. H. Glenchur, H. H. Zinneman and W. H. Hall. A. M. A. Arch. Int. Med. **103**:173-183 (Feb.) 1959 [Chicago].

The recent renewed interest in the general problem of resistance to infections led to the discovery that patients with multiple myeloma are likewise susceptible to recurrent bacterial infections, particularly pneumococcic pneumonia. The authors present their observations on 51 patients with multiple myeloma, who were treated between 1947 and 1957 at the Minneapolis Veterans Administration Hospital. The diagnosis was established in each patient either by biopsy of bone marrow or accessible tumor or by autopsy and serum protein electrophoresis. The 51 patients with multiple myeloma represented 0.05% of 101,956 admissions. Thirty-four of the patients complained of bone pain usually localized to the back. Bone tenderness, the commonest physical finding, was found in 39 patients, mostly over the areas of pathological fractures or myelomatous involvement. Seventeen patients were found to have hepatomegaly at some time during their course. Nine patients had palpable tumors of either the skull, clavicle, sternum, rib, jaw, or pubis. Paraplegia was present in 5 patients. Forty-two of the patients are dead, 8 are living, and 1 has been lost to follow-up.

The authors were impressed with the high incidence of pneumonia. Twenty-eight patients experienced one or more episodes of pneumonia, exclusive of terminal pneumonia, during the course of their disease. A total of 76 episodes of pneumonia was experienced by these patients, averaging 2.7 bouts per patient. Electrophoresis of the serum of the 28 patients with pneumonia revealed only 1 patient with a normal protein pattern. Terminal pneumonia occurred in 17 of the patients. This reflects the increased susceptibility of patients with multiple myeloma to infection, the debilitated state, and the inexorable course of the disease. Seven of the 51 patients experienced bacteremia (14%). This incidence appears higher than chance would permit, and shows that the inability to produce effective antibodies leads to serious infections other than

pneumococcic respiratory infections. Bacteria isolated from the blood included the Staphylococcus and Proteus organisms, Escherichia coli, and Neisseria catarrhalis. Twenty-nine of the patients had infections other than pneumonia, predominantly of the urinary tract. Repeated bacterial infections, especially pneumococcic pneumonia, should be emphasized as an important and often early complication of multiple myeloma. Antibiotics are effective unless their use is delayed.

Idiopathic Pulmonary Haemosiderosis in Adults and Adolescents. D. H. A. Boyd. Brit. J. Dis. Chest 53:41-51 (Jan.) 1959 [London].

Three cases of idiopathic pulmonary hemosiderosis are reported. Two occurred in men, aged 37 and 33 years, and one in a 19-year-old woman. Twenty-nine cases of this condition in persons over 16 years of age were collected from the literature. The more common clinical features were dyspnea, hemoptysis, and anemia; pyrexia, headache, hepatosplenomegaly, abdominal pain, and clubbing of fingers were less common. Natural remissions were frequent and in the author's 2 male patients lasted as long as 18 years and 5 years. The typical roentgenographic abnormality of miliary mottling, usually in the midzone and the lower zone, was almost always present at some stage of the disease. An acute attack may occur without roentgen-ray changes. As the causation of idiopathic pulmonary hemosiderosis remains unknown, effective therapy is lacking. The prognosis is serious. One of the author's 3 patients died, and 19 of the 29 patients reported by others were dead at the time of writing. The most recent work on the pathogenesis of the disease suggests that the elastic fibers of the small blood vessels of the lung are weakened by an increase in acid mucopolysaccharide. An analogy with senile elastosis and arachnodactyly has been drawn by other workers.

Staphylococcal Pneumonia. W. T. Couter. Illinois M. J. 115:57-61 (Feb.) 1959 [Chicago].

Hospital-acquired staphylococcic pneumonia represents a grave danger to life. The so-called "tame" or "hospital" Staphylococcus organism which causes this disease is present in nose and throat cultures of otherwise healthy hospital personnel. Eighty to 95% of physicians, nurses, and attendants harbor staphylococci in the anterior nares, and 60 to 75% of these organisms have been resistant to many antibiotics. The staphylococci may live for months in blankets or mattresses; the air itself acts as a medium of transference, and shaking out the blankets may disseminate the micro-organisms. The existence of such a large reservoir of pathogenic staphylococci renders likely the possibility of staphylococcic parasitization of the hospitalized patient. The widespread use of antibiotics for prophylactic reasons has been held partially responsible for the growing incidence of hospital-acquired staphylococcic disease. A patient entering the hospital with an antibiotic-sensitive strain of staphylococci generally maintains that strain throughout his hospital stay. In contrast, patients receiving either penicillin or a tetracycline tend to become carriers of the staphylococci predominant in that hospital. It seems evident that hospitalized patients, particularly those who receive antibiotics or steroids, can hardly escape from hemolytic staphylococcic colonization.

Staphylococcic pneumonia is a necrotizing process which makes treatment during the first hours mandatory. Sputum and sensitivity studies should be started as soon as a clinical diagnosis of pneumonia have been made, and energetic treatment with antistaphylococcic drugs should be instituted until the diagnosis has been confirmed. As certain strains of staphylococci tend to be constant and predominant in any one hospital, the choice of antibiotics might be determined by data already collected on previous cases by the hospital laboratory. Vigorous treatment by a battery of such antibiotics, to which other staphylococcic cultures have been sensitive, will not endanger the patient if the diagnosis should not be confirmed; in fact, such therapy may save the patient's life.

The Work of Breathing in Patients with Mitral Stenosis. R. Garbagni. Minerva med. 49:4832-4838 (Dec. 22) 1958 (In Italian) [Turin, Italy].

Energy cost of breathing was studied in 10 persons, 7 of whom (aged between 16 and 48 years) had mitral stenosis, and 3 had normal respiratory and cardiovascular functions. Dyspnea on exercise was present in all the patients, and dyspnea at rest in 2. The patients were unable to exert any excessive physical effort. Six patients had sinus rhythm, and one had total arrhythmia attributed to atrial fibrillation. The patients were free from symptoms of widespread cardiac decompensation. Roentgenograms showed an increased shadow either of the whole heart or of the right heart. The patients took 2 or 3 tests of hyperventilation at the breathing frequency of 30 or 40 a minute.

The energy cost of hyperventilation in persons of the control group increased proportionally with higher ventilatory volumes; it deviated from proportionality and became erratic in patients with mitral disease. Among the patients the lowest observed value of the cost of breathing oxygen per liter per minute was 0.53 cc. in a patient with very constricted mitral stenosis, associated with considerable limitation of chest movements caused by kyphoscoliosis. (Energy cost was stated, not in calories or other customary energy units, but in cubic centimeters of oxygen [1000 cc. O_2=4.825 Cal.].) The highest observed value of the cost of breathing oxygen per liter per minute was 12 cc. in a patient

with mitral stenosis accompanied by pulmonary arterial hypertension. Use of the spirometer showed normal ventilatory values in 2 patients and decreased values, ranging from 29 to 41% of the theoretical normal values, in the remaining patients.

Although the scatter of the points on a two-dimensional plane, plotting the values of the energy cost of breathing, was more dispersed for patients with mitral stenosis than for the control group, yet the area containing these scatter points, either of the patients or of the control group, occupied approximately the same position in the diagram. The only exception was the patient with pulmonary arterial hypertension, who exhibited high values of the energy cost of breathing. Similarly, no direct relationship between the increased work of breathing and the degree of severity of a possible cardiovascular disorder could be postulated.

SURGERY

Total Cervical-Spine Fusion for Neck Paralysis. J. Perry and V. L. Nickel. J. Bone & Joint Surg. 41A:37-60 (Jan.) 1959 [Boston].

The authors report on 100 patients with severe paralysis of the cervical muscles with residual instability of the head, who were studied at the Rancho Los Amigos Poliomyelitis Respiratory Center in Downey, Calif.; their object was to formulate a systemic therapeutic plan for those who had regained considerable use of their extremities and now needed a stable head and neck for maximum activity. Close examination of these patients revealed that the muscles of the neck form 4 functional groups, namely, flexors and extensors acting on the head, which were designated "capital flexors" and "capital extensors," and flexors and extensors acting only on the cervical spine, with motion centered in the lower cervical spine, for which the terms "cervical flexors" and "cervical extensors" were coined. Paralysis of the muscles of the neck may prevent the patient's taking advantage of the function that is present in his extremities. Paralysis of the capital extensors may greatly embarrass or completely prevent swallowing and speech by allowing the head to fall into extreme flexion.

Twenty-two fusions of the cervical spine, 10 of which included the skull, were performed at the Rancho Los Amigos Hospital during the past 2½ years. Results showed that total cervical spine fusion is an effective way of replacing the stability essential for general activity, and this fusion must include the occiput if the capital extensors are weak. A halo fixed to the cranium with screws and fastened to an adjustable countertraction device, which has been fixed to the body cast, proved to be a successful means of stabilizing the head and neck for fusion in a predetermined position. With the use of mechanical respiratory aid, the presence of respiratory paralysis is no longer a deterrent to safe major reconstructive surgery.

A Resectable Form of Multiple Mesothelioma. M. S. Harris, M. M. Hyman and D. B. Nevius. Dis. Chest. 35:127-133 (Feb.) 1959 [Chicago].

The authors report on 2 women, aged 43 and 37 years, and a 51-year-old man with multiple mesothelioma of the pleura, for which these patients were operated on. Their cases had certain gross and microscopic characteristics in common. At surgical intervention it was noted that, although the tumors over the parietal surface were quite hard and appeared to involve the underlying soft tissues, bone itself and deep structures were not invaded, and the tumors were movable. The diffusely spread masses could be stripped from the chest wall along with the pleura without resorting to rib resection. Although the frozen section made in the course of the surgical intervention was reported as adenocarcinoma, it was decided, in the case of the first woman, to rely on clinical judgment and to proceed with radical resection. This patient is living and well more than 5 years after the operation. In the case of the man, the frozen section was reported as "papillary adenocarcinoma of the pleura, possibly metastatic, possibly mesothelioma." Because of this report, the situation was deemed hopeless, and the chest was closed. The patient was reoperated on 6 months later, but complete removal of all visible tumor was no longer possible. The pathological diagnosis on the permanent paraffin sections was "mesothelioma of the pleura." The patient died 7 months later, with widespread involvement of the chest wall, mediastinum, and pericardium. In the case of the second woman, a radical pleuropneumonectomy was performed, although the frozen section was reported as adenocarcinoma. The patient is doing well 2 years after the surgical intervention.

The point is raised that the resemblance to adenocarcinoma in frozen sections might lead the surgeon to abandon the surgical intervention in the belief that a hopeless situation exists. It is suggested that the pattern of clinical course, chest roentgenogram findings, and gross findings at surgical intervention should raise the question of a resectable mesothelioma of the pleura, despite a contrary pathological report based on a frozen section. Later, close studies of permanent paraffin sections of the 3 cases in this series were interpreted as mesothelioma because of a differentiation not possible on the frozen-tissue study. These observations emphasize the unreliability of the frozen section in diagnosing mesothelioma of the pleura and the need of clinical awareness of its deceptive appearance both microscopically and grossly.

Lower Esophageal Rings: Report of 14 Cases. J. R. Spencer, R. W. Hammer and W. H. Wierman. Am. Surgeon 25:20-24 (Jan.) 1959 [Baltimore].

The authors direct attention to an abnormality of the distal part of the esophagus, which has been designated as "contractile ring of the lower esophagus" or as "Schatzki ring." They detected it in 14 patients studied in the x-ray department of the Presbyterian Hospital, Denver, in an 18-month period from March, 1956, to September, 1957. Data on these 14 patients are summarized. Only 4 presented the characteristic symptom of intermittent dysphagia; in each of these 4 patients the size of the ring was 13 mm. or less. In 7 patients an esophageal hiatus hernia was demonstrable roentgenologically in association with the ring. Failure to clearly demonstrate such a hernia in the remaining 7 patients does not, however, exclude its presence. Only 2 patients were under 50 years of age, and both of these were without dysphagia. Of the 4 patients with dysphagia, 3 were treated by esophageal dilatation or dietary instructions. The 4th patient was subjected to surgical exploration because of poor response to surgical measures.

The distal part of the esophagus was mobilized, there being no evidence of an esophageal hiatus hernia. Palpation of the esophagus revealed no abnormality except possibly some increased thickening of the wall at the level approximately 4 to 6 cm. above the diaphragm. The esophagus was opened longitudinally at this level. An exploring finger was then inserted into the esophageal lumen and was passed with ease distally into the stomach and proximally. The esophagus was closed in 2 layers without a definitive surgical procedure being performed. The dysphagia disappeared after this exploratory procedure. It is probable that myotomy was performed inadvertently.

The anatomic substrate of the roentgenographic entity of "contractile ring of the lower esophagus" has not been clearly demonstrated, but limited observations suggest either an overactivity or hypertrophy of the inferior esophageal sphincter. The anatomic findings in the few surgically treated patients were conflicting. Only the smaller rings (13 mm. or less in diameter) cause dysphagia; the larger rings are asymptomatic. Conservative treatment provides symptomatic relief in most patients.

Virilizing Tumor of the Adrenal Gland with Pigmentation and Arterial Hypertension Successfully Treated by Surgical Exeresis. P. Mozziconacci, C. Dubost, J. L'Hirondel and others. Semaine hôp. Paris 34:3173-3179 (Dec. 24) 1958 (In French) [Paris].

The authors report on a girl, 2 years of age, with a precocious puberty syndrome. The case was unusual in that manifestations were very early, and there was abnormal pigmentation and arterial hypertension, which intervention caused to disappear. Body hair was heavy and black; external genital organs were quite developed; acne was present on face and back; there was considerable muscular force; the voice was deep and harsh; and bone development was equal to that of a child of 6 years. Androgenic hyperactivity originated in the adrenal gland. Absence of response to corticotropin (ACTH) permitted determining that hyperplasia was not present, and, therefore, a tumor was sought. Much elimination of fraction B of the 17-ketosteroids confirmed the impression. Roentgenologic examination showed a tumor, the size of a grapefruit, which lowered the right kidney. It was removed and found to be a corticoadrenal adenoma. After the operation precautions were taken to avoid a sudden drop in the patient's arterial pressure. Adrenal insufficiency was supplemented with hydrocortisone, cortisone, and desoxycorticosterone. The left adrenal gland was reactivated with ACTH. Fifteen months after intervention the clinical transformation was complete. The child's hair became blond, the skin became fine, and the height and weight increased in normal proportion for age.

The authors suggest that the problem of distinguishing a tumor from hyperplasia of the adrenal gland is partly settled by the criterion of time of appearance of clinical signs. In virilizing tumor, signs are present very early, in this case at birth. In hyperplasia, clinical signs do not appear for several months and frequently not for several years. Absence of response to ACTH and much urinary elimination of dehydroepiandrosterone confirmed the probability of tumor in this case. Hyperpigmentation is generally attributed to excess functioning of the hypophysis, which is no longer checked by cortical secretion. Hypertension in the presence of adrenal gland tumor in a child may be the result of an endocrine mechanism.

Crohn's Disease. A. V. Pollock. Brit. J. Surg. 46:193-206 (Nov.) 1958 [Bristol, England].

In the present study, a group of 34 patients, first reported in 1950, has been reexamined, and the series extended by the addition of all patients with regional ileitis (Crohn's disease) admitted to the Leeds General Infirmary from 1950 to 1956. In all, the cases of 108 patients (48 male and 60 female), ranging in age from 4 to 69 years at time of operation, were reviewed. The author prefers the term "Crohn's disease" because he feels that even the least specific of the noneponymous names is too restrictive to describe a disease which sometimes shows itself in a diffuse and not a regional inflammation. He excluded from this series all patients with lesions not conforming to a provisional definition of Crohn's disease as "a chronic inflammatory disease of the gastrointestinal tract of unknown

etiology, usually manifesting itself in the form of localized thickening of the intestinal wall, with a strong tendency to recurrence which may be more diffuse than the original lesion." This definition excludes cases of solitary ulcers of the jejunum or ileum, intestinal tuberculosis, chronic ulcerative colitis, chronic localized diverticulitis, and intestinal actinomycosis.

In discussing possible relations to other diseases, the author gives particular attention to ulcerative colitis, pointing out that opinions are sharply divided. He presents brief histories of 7 patients in this series, in whom a diagnosis of ulcerative colitis was entertained at some time during the course of the disease. There is evidence that in patients with classical Crohn's disease of the small intestine a diffuse colitis, generally right-sided and resembling nonspecific ulcerative colitis, may develop, and these patients have been considered to be primarily cases of Crohn's disease. When obstruction or fistula complicates Crohn's disease, surgical treatment is indicated. Nothing was found to indicate the superiority of resection in 1 or 2 stages, short-circuiting, or short-circuiting with exclusion of the diseased segment.

Fifty-two of the patients in this series have been followed for more than 5 years, and 30 for more than 10 years. The recurrence rate in patients who had symptoms for more than 2 years before operation, and have been followed for more than 5 years subsequently, was 65%. When the history before operation was less than one month, nearly all the patients recovered permanently, only 12% having suffered a recurrence. When the history before operation was between 1 month and 2 years, 22% of the patients followed for more than 5 years developed a recurrence. In two-thirds of the recurrences, symptoms of recurrence commenced within a year of operation. Once the disease has recurred, it is unlikely to be brought permanently under control by medical or surgical means.

Congenital Coronary Arteriovenous Aneurysm: Clinical, Angiocardiographic and Physiologic Findings on Three Patients with Successful Surgical Correction. B. M. Gasul, E. H. Fell, M. Moreano and M. Weinberg Jr. A. M. A. Arch. Surg. **78**:203-205 (Feb.) 1959 [Chicago].

The authors report on a 7-month-old male infant and on 2 boys, aged 5 and 9 years, with congenital coronary arteriovenous aneurysm draining into the right ventricle, in whom the aneurysmally dilated right coronary artery was successfully ligated and the aneurysm resected. The correct preoperative diagnosis was made in these patients by correlating the clinical findings with those of venous angiocardiography, retrograde aortography, and cardiac catheterization. Corrective surgical treatment is feasible for patients with this rare malformation.

The Surgical Treatment of Marginal Ulcer. J. M. Beal. Am. Surgeon **25**:1-7 (Jan.) 1959 [Baltimore].

Two hundred four patients in whom a diagnosis of marginal ulceration was established were admitted to the New York Hospital from 1932 through 1957. Anastomotic ulceration followed gastrojejunostomy in 151 patients, and it was a sequel of partial gastrectomy in 53. The interval between the primary operation and the appearance of marginal ulceration varied from 2 weeks to 29 years. The peak incidence of secondary ulceration after both partial gastrectomy and gastrojejunostomy was within 1 year of the primary procedure, but in a significant number of patients who had undergone gastrojejunostomy stomal ulceration occurred more than 10 years later.

In 44 of the 151 patients who had undergone gastrojejunostomy, the marginal ulceration was managed without operation. The remaining 107 patients were subjected to a total of 324 surgical procedures. Dismantling of the anastomosis and partial gastrectomy were performed in 62 patients. A second partial gastrectomy was undertaken in 4 of this group for recurrent ulceration, and an additional patient had a transthoracic vagotomy. In 29 patients dismantling of the gastrojejunal anastomosis alone was performed. Resection was performed later in 16 of this group. Eight patients were treated by vagotomy. Later partial gastrectomy was performed in 3 of these. Miscellaneous procedures were employed in 8 patients. Four patients were subjected to revision of the gastrojejunal anastomosis. One patient had a bleeding vessel ligated through a gastrostomy; a gastrojejunocolic fistula was closed in one. The fistula recurred later and was treated by partial gastrectomy. Pyloric exclusion was accomplished in one patient. Recurrent ulceration appeared, and relief of symptoms was obtained by excision of the gastric antrum one year later. Jejunojejunostomy was performed in one patient. Six deaths occurred in the postoperative period—1 after dismantling and resection, 4 after simple dismantling, and 1 after vagotomy. Analysis of the results of treatment of marginal ulcer after gastrojejunostomy demonstrated that there are definite hazards whether conservative or operative treatment is employed. There were 8 postoperative deaths and 5 deaths caused by ulcer in the 107 surgically treated patients, a total mortality of 12.1%. There were 5 deaths from ulcer among the 44 patients treated without operation (11.3% mortality). However, only 4 of this latter group remained free of ulcer symptoms, whereas in the group of patients who were treated by surgical means after the appearance of stomal ulceration, 47 are considered well.

Nineteen of the 53 patients in whom stomal ulceration developed after partial gastrectomy received conservative management. The 34 patients who

were treated surgically had a total of 104 operations. A higher resection was undertaken in 14 patients, with one postoperative death. Seventeen patients were subjected to vagotomy; in 13 a transthoracic approach was employed, and in 4 the vagus nerves were divided by subdiaphragmatic exposure. Miscellaneous procedures were carried out in 3 patients. Of the 19 who were treated by conservative methods, only 2 are free of ulcer symptoms, and 1 has died of complications from ulcer. Of the 34 patients treated by surgical procedures, 14 have remained well for 5 years or longer. Seven patients have been free of ulcer for less than 5 years. Three died from operative intervention in this group of 34 patients. Although the mortality rate was not significantly different for surgical and nonsurgical management, relief from recurrent ulceration was significantly greater in the surgically treated patients.

Dumping Syndrome: Recent Changes in Concept of this Common, Distressing, and Hence Important Postgastrectomy Development. J. W. Butin. J. Kansas M. Soc. 60:1-10 (Jan.) 1959 [Topeka].

Gastric surgery which bypasses or sacrifices the pylorus produces uncomfortable symptoms shortly after meals, called the dumping syndrome. These symptoms may be classified according to probable mechanisms of production as (1) mechanical and (2) vasomotor. Mechanical symptoms are characterized by abdominal fulness, nausea, and, at times, crampy abdominal pain followed by diarrhea. Vasomotor symptoms are characterized by perspiration and feeling of warmth, faintness, and tachycardia. In order to determine the true significance of the dumping symptoms, the author studied 94 consecutive patients who had undergone gastrectomy for benign disease at the Wichita (Kan.) Clinic between 1948 and 1955. The Billroth II operation had been carried out on 41 of the 94 patients, 25 of whom demonstrated dumping symptoms postoperatively; Billroth I operation had been performed on 14 of the 94, 7 of whom showed dumping symptoms after the operation, and the Hofmeister modification of Polya's operation had been carried out on 21, 13 of whom showed dumping symptoms after the operation. The type of operation was not known in 9 of the 94 patients with dumping symptoms. Thus, dumping symptoms were clearly recorded in 45 of the 94 patients.

Analysis of these patients revealed that neither the type of operation nor the amount of stomach resected seemed to reflect a relationship to the dumping syndrome. There is no means by which one can know preoperatively which patient will develop dumping symptoms, nor is there a way by which they can be effectively prevented by modification of the surgical procedure itself. Questionnaires were sent to the first 52 patients whose records contained possible complaints indicating existence of the syndrome. Thirty-six of these patients returned the questionnaires, complaining chiefly of the mechanical symptoms which occurred 30 minutes after eating; they were of the opinion that excessive food intake or excessive exercise after meals would produce these symptoms. Most common offending foods were dairy products, sweets, and any liquids taken with meals. Twenty-three of the 36 patients still had dumping symptoms at the time the questionnaire was filled out from 1 to 5 years after gastrectomy, and 18 of these patients indicated that the symptoms occurred often enough to be considered significant.

The most attractive theories of etiology of the syndrome are based on the relationship of osmotic pressures within the jejunum to those within the blood. The osmotic pressures can be increased by ingestion of foods which are hypertonic, especially if sufficient liquid is consumed to dissolve them. Such osmotic energy can be dispersed by vomiting, by diarrhea, or by reclining of the patient which produces a reflux of the meal into the gastric remnant. However, unless such dispersal of osmotic pressures occurs, a sudden shift of extracellular fluid from the blood to the jejunum results, which equalizes osmotic relationships between the 2 areas. The resultant decrease in blood volume is accompanied in certain individuals by a marked peripheral vasodilatation which results in pooling of blood away from the central areas, such as the heart and brain. The vast amount of fluid entering the jejunum itself produces distention and the mechanical phase of symptomatology, whereas the vasomotor symptoms are mediated through the autonomic nervous system, discharges of which seem to be initiated by acute changes in the circulating blood volume.

Satisfactory medical treatment of the dumping syndrome is based on dietary manipulation. Sweets, fluids, and dairy products are avoided with meals. Rest in the reclining position is advised after an unavoidably large meal. Small frequent feedings are preferable, especially in the early postoperative period. It is felt that apparent spontaneous improvement of the patient with the postgastrectomy syndrome usually reflects a process of self-education. The physician who understands the physiological mechanisms of this postgastrectomy syndrome can often lead his patients quickly to a remission of these troublesome symptoms.

Hirschsprung's Disease: Nine Years' Experience at the Hospital for Sick Children, Toronto. B. Langer and S. Thomson. Canad. J. Surg. 2:123-130 (Jan.) 1959 [Toronto].

While congenital megacolon (Hirschsprung's disease) has been recognized as a disease entity for well over 70 years, it is only in the past 15 years

that a satisfactory concept of its etiology and treatment evolved. The authors review the development of the present concept of this disease, pointing out that it was not until 1948 that Swenson correlated the pathological findings with x-ray observations and, in addition, carried out motility studies. The primary defect is a congenital maldevelopment of the innervation to the undilated segment of the intestine, which is recognizable on pathological examination by absence or scarcity of ganglion cells in the myenteric plexus, and is usually accompanied by an increase in the number of nonmyelinated nerve fibers. Swenson stated that this defect in innervation was responsible for the failure of this part of the intestine to expand or transmit peristaltic waves in a normal fashion, thus producing a physiological obstruction with resulting proximal dilatation and hypertrophy. With recognition of the aganglionic segment as the diseased part of the intestine, Swenson also developed a method of excising it as far as the anus and of anastomosing ganglion-containing intestine to anus by a pull-through procedure. This operation has now replaced all other procedures in the treatment of the disease.

The authors report studies on 58 children with Hirschsprung's disease observed at the Hospital for Sick Children at the University of Toronto from 1949 to 1958. The diagnosis was verified in most of these children on the basis of pathological material. As in other reported series, there was a marked predominance of males (46 boys and 12 girls). The age at which symptoms brought these children to the hospital for the first time varied from 1 day to 6 years. The problem of diagnosis in the newborn infant is reflected in the fact that, of the 20 children seen during the first week of life, the correct diagnosis was made within a week of admission in only 5. Of the remaining 15, the condition of 5 was recognized at postmortem examination, and that of 10 was diagnosed after a period varying from 2 weeks to 6½ years. The provisional diagnoses included unspecified intestinal obstruction, meconium ileus, congenital anal stenosis, gastroenteritis, and pyloric stenosis. There were 20 deaths, but only 8 were postoperative deaths; 4 of these 8 children were moribund at the time of operation. Twelve of the 13 patients who were not subjected to a suitable operation died. With a better understanding of Hirschsprung's disease, the diagnosis is being made with greater frequency and earlier in the course of the disease. The main adjuncts to clinical diagnosis are special x-ray methods of visualizing the colon and pathological examination by rectal biopsy.

Surgical treatment is advisable in all cases. At the authors' hospital the first pull-through procedure was done in 1949, and since then a total of 22 patients with Hirschsprung's disease proved by pathological examination have undergone operation. The age at time of operation varied from 1 month to 11 years. In the early 1950's the pull-through operation was a primary procedure, without preliminary colostomy, at any age from one month on, if the patient's condition permitted. During recent years the practice has been to perform a primary pull-through operation only on older children (over 2 years of age) who are in good condition. On all others a preliminary defunctioning colostomy is done above the aganglionic segment, the definite operation being delayed until the infants reach at least 20 to 25 lb. in weight.

NEUROLOGY & PSYCHIATRY

Attempt at a Classification of Postoperative Deliriums: A Physiopathological and Therapeutic Synthesis. P. Chalnot, P. Michon, J. Sommelet and others. Semaine hôp. Paris 35:8-12 (Jan. 4) 1959 (In French) [Paris].

The authors differentiate between the postoperative delirium associated with alcoholism (delirium tremens), which is usually related to alcohol withdrawal and possibly to hyperkalemia, and the postoperative deliriums which are essentially connected with hydroelectrolytic disorders occurring in nonalcoholic subjects. Study was carried out by means of clinical data, biological values, and determination of neuromuscular excitability in 18 patients. In postoperative delirium tremens, a widespread neuromuscular hyperexcitability, in which muscle is more excitable than nerve, was consistently found. It is probable that hyperkalemia with cellular hyperhydration constitutes the most important biological fact in postoperative delirium tremens.

The varieties of postoperative delirium which are connected with metabolic hydroelectrolytic disturbances are as follows: delirium with extracellular dehydration, hypokalemia, and cellular sodium intoxication; delirium with extracellular dehydration, increased osmotic pressure, and excessive electrolytes in the blood; delirium with cellular hyperhydration and water intoxication, which is usually the result of an excessive and badly directed treatment; delirium with multiple electrolytic losses and preponderant sodium loss; delirium with alkalosis; and delirium with multiple deficiencies. These distinctions between types of delirium allow use of an adapted therapy. Any therapy not explicitly directed risks being not only inefficacious but also dangerous. True postoperative delirium tremens reacts well to the anesthetic steroid, hydroxydione sodium succinate (Viadril). Correct hydration, sufficient caloric support, and administration of strong doses of vitamin B_1 and magnesium sulfate are associated with this therapy. For electrolytic disturbances the authors use a combined preparation

of levulose, insulin, and potassium, or hypertonic salt solutes and desoxycorticosterone acetate, or a reduced water intake according to the case.

There is always the possibility that different varieties of postoperative delirium will succeed each other in the same individual. Therefore, a daily water balance and often a series of apparently contrasting therapies are necessary. Research should continue along the lines of clinical study, evaluation of electrolytes in the serum, water balance, and determination of neuromuscular excitability.

Central Pontine Myelinolysis: A Hitherto Undescribed Disease Occurring in Alcoholic and Malnourished Patients. R. D. Adams, M. Victor and E. L. Mancall. A. M. A. Arch. Neurol. & Psychiat. 81:154-172 (Feb.) 1959 [Chicago].

The authors report on 3 alcoholic patients (2 men, aged 38 and 43 years, and a 29-year-old woman) and on a severely malnourished 53-year-old woman with a single pathological entity for which the term "central pontine myelonolysis" was chosen. These patients had been admitted to the Boston City Hospital where they died. Autopsy revealed a single, sharply outlined focus of myelin destruction, which was localized in the rostral part of the pons and indiscriminately affected all the fiber tracts. The axis cylinders and nerve cells were largely spared, and there were no inflammatory or vascular changes. The process probably began in the central portion of the pons and spread in a centrifugal manner, disposing itself symmetrically about the midline. In the 38-year-old man and in the 29-year-old woman with the largest lesions, the disease had manifested itself clinically by a pseudobulbar palsy and rapidly evolving flaccid quadriplegia, with weakness of the face and tongue and an inability to speak and swallow, leading to death in about 13 and 26 days. In the other 2 patients there were no symptoms referable to the lesions, presumably because of their small size. The condition did not resemble vascular diseases of the brain stem, Wernicke's superior hemorrhagic polioencephalitis, degeneration of the corpus callosum (Marchiafava-Bignami's disease), multiple sclerosis and related disorders. No reference to a disease of the described type has been found in the medical literature of the past 75 years.

The causation of central potine myelinolysis is unknown. Occurring on a background of alcoholism and malnutrition, the nature and location of the disease favor either an exogenous or an endogenous intoxication, or a deficiency of some substance essential to the metabolism of nerve tissue. This hitherto undescribed disease deserves a special name because of its unique clinical and pathological features; it has been designated as central pontine myelinolysis because this term denotes both the specific anatomic localization of this disease and the remarkable unsystematic dissolution of medullated fibers. This description seems preferable to pontine demyelination for 2 reasons. First, demyelination appears to represent only one phase in the course of this disease. In the central part of each lesion, what had begun as a demyelinative process eventually resulted in a destruction of all elements, even the supporting tissues, with resulting cavitation. Second, the term "demyelination" has been applied to a diversity of diseases, usually connoting multiple sclerosis and related disorders, and therefore has come to lack precision.

GYNECOLOGY & OBSTETRICS

Mesenchymal Sarcoma of the Uterus. W. B. Ober and H. M. M. Tovell. Am. J. Obst. & Gynec. 77:246-268 (Feb.) 1959 [St. Louis].

One of the authors had suggested in a previous study a four-group classification of uterine sarcoma: (1) leiomyosarcoma, (2) mesenchymal sarcoma, (3) blood vessel sarcoma, and (4) lmyphoma. In this paper the authors excluded all leiomyosarcomas, the most frequent form of uterine sarcoma. The total of 29 cases, on which this report is based, included, in addition to 26 cases of mesenchymal uterine sarcoma, 1 case of hemangiosarcoma and 2 of lymphoma. The 26 cases of mesenchymal sarcoma, of which 25 were followed up, are classified into 4 categories according to whether their cellular components are pure, mixed, homologous, or heterologous in origin. "Pure" sarcoma signifies one composed of one cell type only; "mixed," composed of more than one cell type; "homologous," containing tissue elements indigenous to the uterus; "heterologous," containing tissue elements foreign to the uterus. Irrespective of cell composition, all members of this family of tumors can be traced to an origin from derivatives of the mesenchyme of the urogenital ridge, specifically that derived from and surrounding the epithelium of the Müllerian duct.

The pure homologous sarcomas occur in younger women, often premenopausal; they grow slowly, metastasize late, if at all, and pursue an indolent clinical course. Total hysterectomy followed by radiation therapy, as indicated, affords a reasonable prognosis for a long-term survival. The pure and the mixed sarcomas, whether homologous or heterologous, occur in older women, usually postmenopausal; they grow rapidly, metastasize widely, and afford limited opportunities for treatment with hope of cure. Over 50% of patients with these varieties of sarcoma die within 2 years, and less than 10% can be listed as 5-year survivals. The

majority of survivors in this group have tumors which are polypoid and exophytic and invade the underlying myometrium superficially, if at all.

Metastases in cases of carcinosarcoma were usually of the carcinomatous component. In one patient the metastasis contained admixed carcinomatous and sarcomatous components. In another patient there was dissociation of the cellular components in the metastases, the ovary containing metastatic adenocarcinoma and a vaginal nodule containing pure metastatic sarcoma. In 10 of 25 cases a prominent clinical feature was a large polypoid mass protruding through a dilated cervical os in a postmenopausal woman whose presenting symptom was uterine bleeding. To some extent, length of survival was correlated with duration of symptoms prior to treatment. Excluding the pure homologous sarcomas, in 14 patients who are dead, the average duration of symptoms was 9.6 months, and the average survival time was 8.2 months; in 7 patients alive at the time of reporting, the average duration of symptoms was 2.3 months, and the average survival time was 39.6 months.

Treatment of patients with carcinosarcoma or mixed mesenchymal sarcoma must depend upon the extent of the disease at the time of diagnosis. If the tumor is polypoid and confined to the endometrium or has only superficially invaded the myometrium, total abdominal hysterectomy with bilateral salpingo-oophorectomy is sufficient. With extension beyond these limits, the prognosis is generally poor, and a course of supervoltage irradiation to the pelvis for palliative purposes is indicated. No results are reported with patients treated by radical hysterectomy, exenterative surgery, or chemotherapeutic compounds. The prognosis appears to be hopeless in the presence of extrapelvic disease.

The Histogenesis of Carcinosarcoma (Mixed Mesodermal Turmor) of the Uterus as Revealed by Tissue Culture Studies. A. Rubin. Am. J. Obst. & Gynec. 77:269-274 (Feb.) 1959 [St. Louis].

The histogenesis of carcinosarcoma of the uterus is obscure. Hence, because of divergent points of view, the study of carcinosarcoma grown in tissue cultures, where elements of exudation, inflammation, compression of cells, vascularity, tumor bed, and host response are absent, seemed to be a logical technique for attempting to learn more about such tumors. The author presents the history of a 57-year-old woman from whom a carcinosarcoma (mixed mesodermal tumor) of the uterus was removed. Two and one-half months after the operation the patient complained of vomiting and weight loss. Large abdominal masses were palpable. In the midvagina there were several friable, polypoid lesions. A similar mass protruded from the urethral meatus. Biopsy specimens of the vaginal and urethral tumors were used to prepare tissue cultures and microscopic sections. The microscopic picture was identical with that of the original uterine lesion. The patient was readmitted and given a course of nitrogen mustard intravenously. The abdominal mass appeared to grow smaller. No effect upon the urethral or vaginal lesions was noted. The patient died 4 months after hysterectomy.

In the tissue cultures prepared from biopsy specimens, 2 distinct cell types were distinguished. One cell type had the characteristics of carcinoma, the other of sarcoma. No intermediate cell types of evidence of transition from one form to the other were seen. These observations lend support to the thesis that carcinosarcoma is a distinct pathological entity in which carcinomatous and sarcomatous elements coexist, rather than merely an atypical or pleomorphic carcinoma. This is the first description of a human carcinosarcoma grown in tissue culture.

Syphilitic Foetus After Prenatal Penicillin Therapy. J. A. Burgess. Brit. J. Ven. Dis. 34:240 (Dec.) 1958 [London].

The prevention of congenital syphilis by the treatment of syphilitic pregnant women has been so successful that clinical manifestations of the disease in infants, after adequate prenatal penicillin therapy, are now seldom seen. In a 32-year-old woman, who attended an antenatal clinic, serological tests for syphilis were positive, the first positive report being obtained during the 16th week of pregnancy. Fetal movements ceased during the 21st week. Crystalline sodium penicillin in a daily dose of 1 million units was given for 15 days, beginning with the 22nd week of pregnancy. In the 27th week miscarriage of a macerated fetus occurred. A postmortem examination of the fetal liver, stained by Levaditi's method, showed the presence of numerous spirochetes which had the morphology of Treponema pallidum. Examination of the husband showed that he had late latent syphilis. It is suggested that antisyphilitic treatment should be given immediately to expectant mothers in whom the initial serologic tests for syphilis are unequivocally positive.

Vaginitis and Pathological States of Newborn Infants: Etiology of Infection with Staphylococci in Newborn Infants. J. Bret and C. Coupe. Presse méd. 67:216-217 (Jan. 31) 1959 (In French) [Paris].

Cultures were obtained from the vaginal canal of 300 parturients and from the nasal cavaties, mouths, and urine of their newborn infants so as to investigate possible transmission of pathogenic

micro-organisms at delivery. Cultures were recovered from 200 women at delivery and from their newborn infants at birth and 6 hours, 24 hours, and 4 days after birth. Cultures were recovered from the remaining 100 women at admission and at delivery and from their newborn infants 24 hours, 4 days, 10 days, and 26 days after birth. Staphylococcus pyogenes var. aureus was recovered in the cultures of 46 women (15%) at delivery. Thirty-seven newborn infants (12%) were found to carry staphylococcus organisms at birth and 10 days afterwards. These organisms were present alone in 10 instances and were associated with either gram-negative bacteria or Candida albicans in 17 instances. Consequently, 37 of 46 mothers (or 82%) who carried pathogenic organisms at delivery transmitted them to their newborn infants. In 9 instances, in which labor was of short duration or in which a cesarean section was performed, the newborn infants were free of pathogenic organisms, although the organisms were present in the mothers. The presence of staphylococci was not observed in those infants whose mothers' vaginas were free of these organisms. Of 100 infants who were inspected on discharge, pathogenic micro-organisms were present in 27; 12 of them were infected at birth, and 15 after birth. This means that 47% of the infections took place at delivery.

Spontaneous disappearance of Staph. pyogenes var. aureus was observed in 4 infants (27%), and of C. albicans in 10 (60%). Of 14 infants who still carried pathogenic organisms 4 days after birth, 7 were affected with the following pathological states: purulent conjunctivitis (2), subcutaneous abscess (1), purulent rhinitis (1), parotitis attributed to staphylococci (1), and suppurative omphalitis (2). The micro-organisms observed in the foci of infection of these infants were of the same type as those identified in their respective mothers at delivery. To prevent transmission of pathogenic micro-organisms from parturients to newborn infants, prophylaxis and treatment for vaginitis of pregnant women, coupled with rigid control of nursery sterility, are recommended.

Sarcoma of the Uterus: A Report of 34 Cases. E. J. Crawford, Jr. and R. Tucker. Am. J. Obst. & Gynec. 77:286-291 (Feb.) 1959 [St. Louis].

This study was undertaken to correlate the clinical findings, diagnosis, management, and ultimate outcome in 34 patients with uterine sarcoma, who were seen during the 9-year period from 1948 to 1956 at 2 hospitals in Shreveport, La. One of the hospitals is a charity institution and a referral center; the other is a private hospital. Sarcomas constituted 2.6% of all uterine malignancies. Twenty-six of the patients had leiomyosarcoma; in 6 the leiomyosarcoma was primary (arising in the myometrium), and in 20 it was secondary (arising in a myoma). Of the other 8 patients, 3 had endometrial stromal-cell sarcoma, and 5 had mixed mesodermal tumors. The average age of the patients with leiomyosarcoma was less than 50 years; for those with the other 2 forms of sarcoma it was over 67 years. The majority of the patients had the triad of irregular bleeding, abdominal mass, and lower abdominal pain. These symptoms are not characteristic and are similar to those of other benign and malignant diseases of the uterus. The only preoperative diagnoses were made from curettement or biopsy. Two patients had tumors of the cervix, and diagnosis was made from biopsy. Two other patients had necrotic tissue in the vaginal vault, from which diagnosis was established. A diagnostic curettage was done 8 times in the patients with leiomyosarcoma; 3 cases were reported positive. In the endometrial stromal type the curettement yielded a positive diagnosis in all cases. In the mixed mesodermal tumors a curettement was done in 2 cases, and both were positive. The diagnosis of leiomyosarcoma was usually made on histological examination of the surgical specimen.

Three of the 26 patients with leiomyosarcoma were found to have inoperable disease. Sixteen of the remaining 23 patients were treated by total abdominal hysterectomy; 7 of them died, and 9 are living from 2 to 8 years after the hysterectomy. Of the 6 patients who underwent subtotal hysterectomy, 4 are dead, and 2 are alive more than 5 years after the operation. One patient who was treated by vaginal hysterectomy is still alive (3 years later). Operation was the treatment of choice. The operative mortality was 3.8%. Irradiation was of doubtful benefit. The extent of the tumor was the most important factor in prognosis. All the patients in whom the sarcoma extended outside the uterus are dead. Earlier diagnosis may possibly increase the survival rate. The 5-year survival rate in this series was 26.5%. There were no 5-year survivors in the endometrial stromal-cell and mixed mesodermal groups. The leiomyosarcoma arising in a fibromyoma seems to be the most favorable type of sarcoma.

PEDIATRICS

The Relationship Between Bronchiolitis and Childhood Asthma: A Follow-up Study of 100 Cases of Bronchiolitis. H. J. Wittig and J. Glaser. J. Allergy 30:19-23 (Jan.-Feb.) 1959 [St. Louis].

The high incidence of respiratory allergies in children with a history of bronchiolitis could be of significance for an etiological relationship between bronchiolitis and asthma. This prompted the authors to study 100 children with acute bronchiolitis admitted to the pediatric services of 3

major hospitals in Rochester, N. Y., between 1950 and 1957. The patients' ages ranged from 4 weeks to 4 years. Seventy-six patients were under the age of one year. The purpose of this study was to ascertain in how many of these 100 children bronchial asthma or other respiratory allergies developed subsequently and how many had a positive family history for allergy. Studies of hospital records and communication with the patients' families and their private physicians indicated that in 32 children bronchial asthma and in 17 upper respiratory disorders, perennial allergic rhinitis, or pollinosis developed subsequently. The diagnosis of asthma in the 32 children was made between 1½ and 2½ years after their original admission to the hospital with acute bronchiolitis. A reliable family history was available for only 83 of the 100 patients; 37 of these showed incidence of either asthma, pollinosis, or eczema. It seems fair to assume that acute bronchiolitis in infancy should be looked upon as a condition which is often followed by the development of respiratory allergic disease, particularly asthma, and appropriate prophylactic measures should be instituted.

Disturbances of Acid-base Equilibrium in Salicylate Intoxication. R. W. Winters, J. S. White, M. C. Hughes and N. K. Ordway. Pediatrics **23:** 260-285 (Feb.) 1959 [Springfield, Ill.].

The 33 patients with salicylate intoxication reported ranged in age from 2 months to 19 years, but most of them were 3 years of age or less. Salicylate had been taken in the form of aspirin by 31 of the patients and in the form of methyl salicylate or phenyl salicylate by 1 patient each. In 16 instances the salicylate was accidently ingested; a 19-year-old girl had ingested aspirin in a suicidal attempt; in the remaining 16 persons poisoning resulted from therapeutic overdosage in the treatment of febrile respiratory infection, acute rheumatic fever, or rheumatoid arthritis. The total carbon dioxide content of the blood and the carbon dioxide tension (pCO_2) of the plasma were significantly reduced in nearly all the patients. The pH of the blood did not vary consistently: some patients were alkalotic, others were acidotic, while still others had no significant deviation in pH of the blood. There was evidence that many patients had a mixed disturbance in acid-base equilibrium, with primary disturbances in the metabolic and the respiratory components.

The nature of the metabolic acidosis was analyzed by a detailed study of the anions in the serum of 5 patients with this disturbance. A variety of anions, such as chloride, salicylate, and an undetermined anion, were present in excess; in one patient the concentration of phosphate was likewise elevated. There are indications that ketone bodies account largely for the undetermined anion fraction. The return to normal acid-base equilibrium was studied in 6 patients who presented with an acid pH. This group showed a tendency to recover through a point at which the pH of the blood was normal or even alkaline although the carbon dioxide tension was still low.

In 2 patients who initially presented with an acid pH, acute respiratory depression supervened after acute pulmonary edema. The respiratory depression was accompanied by a marked elevation of the carbon dioxide tension and a marked fall in the pH. One of these patients died; in the other ventilation was achieved by artificial means, and recovery resulted. The authors review the basic effects of toxic doses of salicylate: respiratory stimulation, changes in the metabolic rate, and disturbances in the metabolism of carbohydrate, protein, and fat. The pathogenesis of the acid-base disturbances is formulated in terms of these actions of toxic amounts of salicylate. Several factors may be important conditioning influences in the particular type of disturbance which develops in an individual patient. These factors are the age of the patient, duration of intoxication, type of intoxication (i. e., whether accidental or the result of therapeutic overdosage), and, perhaps, the amount of salicylate ingested.

Evaluation of the Efficacy of Lavage and Induced Emesis in Treatment of Salicylate Poisoning. F. J. Arnold, J. B. Hodges and R. A. Barta. Pediatrics **23:**286-301 (Feb.) 1959 [Springfield, Ill.].

Since the authors recovered only minimal amounts of salicylate by gastric lavage in children with aspirin (acetylsalicylic acid) poisoning, they made experiments in dogs to ascertain the therapeutic value of gastric lavage and to compare it with the effect of emesis. Fasting dogs, 6 to 10 kg. in weight, were given sodium salicylate in tablet form in doses of 0.5 Gm. per kilogram of body weight, and lavage was performed or emesis induced at varying time intervals after ingestion. The lavage and emesis fluids were examined for the amounts of salicylate they contained.

It was found that in the recovery of the ingested salicylate the initial aspiration of the stomach before the introduction of the lavage fluid is equally as important as the succeeding lavage. Lavage carried out within 15 minutes is no more effective than emesis induced within 30 minutes of ingestion. Lavage carried out one hour after ingestion is inefficient and far less effective than emesis produced within the same time interval. Spontaneous emesis is not as effective as induced emesis. Emesis induced immediately, or even when delayed as long as 1½ hours after ingestion, appeared to be the more effective, and thus the preferable, form

of therapy. Neither lavage nor emesis under the most optimal conditions was consistent in effectiveness, so that all patients after either form of therapy should be watched carefully for signs of increasing drug intoxication and should be treated if a specific form of therapy is available.

Serial Study of Bone Marrow in Hemolytic Disease of the Newborn (Erythroblastosis Fetalis). H. C. Dillon and W. Krivit. Pediatrics **23**:314-322 (Feb.) 1959 [Springfield, Ill.].

Fourteen infants with erythroblastosis fetalis were studied, with particular reference to bone marrow activity and its relation to their anemia. Serial studies of the marrow were done in 12 of the 14 infants, and single specimens were examined in 2 infants. The purpose of this study was to determine the relationship between the degree of anemia and the normoblastic activity of bone marrow, as ascertained by morphologic techniques. On the basis of literature reports and the observations in this series of infants, true "aregenerative anemia" appears to be a rare occurrence. To suggest that the anemia of erythroblastosis is commonly due to a cessation of erythropoiesis seems totally unjustified, because these infants show hyperplasia of the marrow which is analogous to that seen in other compensated hemolytic anemias.

Hyman and Sturgeon had stated, and the authors agree, that a relative hypoplasia may occur as cell destruction exceeds cell production. This does not necessarily imply marrow failure or an "aregenerative state," but it may indicate that the balance can be in favor of blood destruction, and an anemia of some degree is the result. In a previous report, infants after exchange transfusion did show excessive destruction of donor erythrocytes. The rate of destruction of Rh-negative cells in erythroblastosis fetalis was twice that of normal. Some of the cases reported in the literature as "aregenerative anemia" lack adequate marrow studies and cannot be accepted as proved. It should be emphasized that it may be unwise to conjecture about the activity of the bone marrow from reticulocyte studies of the peripheral blood alone. In this series, the percentage of normoblasts in the bone marrow was increased in proportion to the degree of anemia.

The Problem of Early Diagnosis of Purulent Meningitis in the Nursling. G. Rottini. Minerva pediat. **10**:1388-1398 (Nov. 24) 1958 (In Italian) [Turin, Italy].

The time of onset of various symptoms of purulent meningitis was studied in 51 nursing infants, 3 days to 12 months old, who were observed during a 5-year period. The significant symptoms of the disease had developed by the 4th or 5th day of illness. A temperature of 39 C (102.2 F) or over appeared on the first day in 23 children; in 10 children the temperature was 38 to 39 C (100.4 to 102.2 F), and in 10 others it was 37 to 38 C (98.6 to 100.4 F). Fever was most frequent in those close to one year of age. Early symptoms of intracranial hypertension appeared in a pattern inversely proportional to the ages of the children; on the first day these symptoms were most frequent and marked in infants, 9 to 12 months old; by the 4th or 5th day they had developed in most of the children. Early symptoms of meningeal irritation were most frequent in infants, 9 to 12 months old; second in frequency were the meningeal symptoms of infants ranging in age from birth to 3 months, followed by those in the age groups of 3 to 6 months and 6 to 9 months. Symptoms of brain involvement were most frequent in the youngest children, being present in 60 to 75% of the children within the first 48 hours of illness. The frequency of early symptoms of neurovegetative involvement increased in a pattern directly proportional to the ages of the children; 10 of the youngest children refused food on the first day of illness, and by the second day one-third of the children refused to eat. The author observed an almost constant association of symptoms of cerebral involvement and of purulent meningitis in these infants.

Still's Disease and Its Nosologic Limits. G. Verdura, N. Svilokos and L. Serafini. Minerva pediat. **10**: 1251-1267 (Nov. 10) 1958 (In Italian) [Turin, Italy].

The authors report on a boy, 4 years of age, with Still's disease. The first episode of the disease, consisting of high intermittent fever and rash, appeared at the age of 11 months. These symptoms recurred intermittently for a few days once a week. Early signs of fixation in flexion of the hands and legs were interpreted as manifestations of spasmophilia and, then, of arthritis. Administration of preparations of calcium, antibiotics, and antipyretics brought no benefit to the child. The subsequent signs and symptoms were progressive pallor, stationary body weight, and failure to develop walking capacity. A pleurisy with effusion was roentgenologically identified and cured in a few weeks. After 2 months of apparent improvement, when the child was 19 months of age, an episode of high fever, enlargement of the vertebrae in the lower section of the spinal column, pain on passive flexion, a marked degree of anemia, and deterioration of the general condition developed. The child was then referred to the clinic, with which the authors are associated, with the diagnosis of spondylitis. On admission the child appeared dystrophic, with very pale, inelastic skin, enlarged joints, muscular atrophy, fixation in flexion of the legs, enlarged and painless spleen, enlarged penis and scrotum

but with testes normal in size. During hospitalization the child received successive therapies with antibiotics as well as Butazolidin, prednisone, and corticotropin (ACTH). Each therapy brought about slight improvement of the symptoms but failed to arrest recurrences. The therapy with isonicotinic acid, administered in daily doses of 20 mg. per kilogram of body weight for 10 months, arrested the recurrence of the disease and produced remission of all symptoms with the exception of a slight rigidity of head movement.

UROLOGY

Wilms's Tumor: A Report of 71 Cases. J. K. Lattimer, M. M. Melicow and A. C. Uson. J. Urol. 80:401-416 (Dec.) 1958 [Baltimore].

Wilms's tumor (nephroblastoma), one of the commonest neoplasms in childhood, apparently needs no longer be regarded as a hopeless disease. This is suggested by the findings in this review of 71 cases (67 proved), from the files of the pediatric urologic service of the Squier Clinic and the Babies Hospital in New York, from 1895 through 1956. "Abdominal mass" was the presenting symptom in 60% of the patients. Vomiting, abdominal pain, fever, or hematuria occurred in some of the children. Hypertension was found in 60% of those patients in whom the blood pressure was recorded. The erythrocyte sedimentation rate was determined in 20 patients, and of 11, in whom the range was high (35 to 90 mm. during the first hour), none survived. The urographic study was the most important single procedure in confirming the clinical impression of nephroblastoma.

Of the 25 patients treated before 1934, only 2 survived, whereas of the 42 treated between 1934 and 1956, 16 have survived 2 years or more. Preoperative irradiation proved unsatisfactory in the 4 patients in whom the full course was given. Better results were obtained with prompt nephrectomy and postoperative irradiation. Thirty-six of the last 42 patients were treated by nephrectomy, and of these 16 survived, 5 surviving so far from 2 to 5 years, 5 from 5 to 10 years, and the remaining 6 from 10 to 23 years. Patients who survived beyond 2 years usually continued to do well. Eighty-five per cent of the children who died after nephrectomy for nephroblastoma succumbed within 2 years.

The age of the patient at the time of surgery was an important factor in prognosis. Of those operated on during the first 2 years of life, 73.3% are alive, whereas only 18.5% of those operated on between the ages of 3 and 9 years are alive. Other factors important for a favorable prognosis were location of the tumor at the lower pole of the kidney, removal of the tumor with the capsule intact, and the absence of invasion or metastases. The prognosis was unfavorable when the child was older, when the tumor was on the upper pole, when the capsule was torn or had been penetrated by the tumor, when invasion or metastases were present, and when the erythrocyte sedimentation rate was above 35mm. during the first hour.

Aneurysm of Renal Artery: Report of Five Cases. B. R. Harrow and J. A. Sloane. J. Urol. 81:35-41 (Jan.) 1959 [Baltimore].

Since previous presentations, including comprehensive surveys, have discussed the etiology, symptomatology, and pathogenesis of aneurysm of the renal artery, the authors in this report add 5 new cases of saccular aneurysms, consider the indications for aortography, and discuss the treatment. Calcific shadows typical of renal artery aneurysms were observed in all 5 patients. In 1 of the 5 patients the aneurysm developed in a solitary kidney, the third instance of this sort reported in the literature. In another patient in whom an excretory urogram revealed 2 small calcific rings, 0.5 and 1.1 cm. in diameter, in the upper pole of the right kidney, suggestive of 2 renal artery aneurysms, a translumbar aortogram confirmed the diagnosis.

Noncalcified aneurysms of the renal artery have a high incidence of rupture, as proved by a survey of the literature. The noncalcific lesion is diagnosed only by aortography, operation, or autopsy. It has been discovered preoperatively with the use of translumbar aortography for hypertension, poorly or nonfunctioning kidneys, or unexplained extra renal or intrarenal noncalcified, space-occupying lesions. Operative intervention to prevent rupture and other complications is necessary in patients with nonopaque saccular aneurysms. Contrary to many previous reports, the authors believe that operation may be unnecessary with large and small calcified aneurysms in asymptomatic, normotensive, elderly individuals. Surgery is indicated if pain, hematuria, hypertension, or renal impairment occurs, and in youthful or pregnant patients.

With regard to aortography in the diagnosis of calcific rings, the authors say that the typical cracked-eggshell appearance of the usual ring shadow, located in the renal hilus on anteroposterior and oblique views, is so characteristic that usually aortography is unnecessary for diagnosis. With an atypical calcification, translumbar aortography is necessary to distinguish among aneurysms, calcified lymph nodes, cysts, neoplasms, old traumatic hematomas, and tuberculomas. The serious complications that have been known to occur in translumbar aortography can be avoided if the proper technique is employed. The authors demonstrate also that the intelligent use of adequate,

closely supervised application of pressure to the abdominal wall during intravenous urography often eliminates the necessity of retrograde pyelography.

INDUSTRIAL MEDICINE

Long-Term Experience with Beryllium Disease: A Report of Twenty Patients. E. M. Kline and T. W. Moir. A. M. A. Arch. Indust. Health 19:104-109 (Feb.) 1959 [Chicago].

A report is presented on 20 patients with chronic beryllium disease who were followed up for 5 years. There were 7 men and 13 women, ranging in age from 25 to 44 years. Five persons were employed in the mixing and firing of zinc beryllium silicate lamp phosphor, and were exposed not only to zinc beryllium silicate but also to the dusts of beryllium oxide. Fifteen persons were employed in lamp factories where the fluorescent tubes were coated, lehred, based, inspected, and packaged for distribution to the consumer; the exposure of these persons was minimal. The data collected indicate that there was not only a quantitative but also a qualitative difference in exposure between the 2 groups. In the first group the average duration of exposure was only 12 months, as compared with the second group whose average exposure in the lamp factories was nearly twice that time (23 months). The average latent period of 2.9 years for the group exposed in the chemical plants was approximately half as great as that for the group exposed during the lamp manufacturing process. The differences in the attack rate, in the duration of exposure, and in the period of delay between the 2 groups are not readily explained by a sensitivity reaction, as suggested by other authors, but are rather indicative of differences in quantity and form of the disease-producing substance of beryllium.

Five patients of the first group received no specific treatment; 2 died, and the other 3 are in a bad condition. The 15 patients of the second group were treated with corticotropin, corticosteroids, or a combination of these agents in an average daily dose of 75 mg. (ranging from 25 to 150 mg.) for an average period of 4.5 years (ranging from 0.8 to 7.5 years). Striking but only transitory improvement has been obtained with corticotropin (or with corticosteroids) in some patients. The favorable response was particularly impressive in patients with rapid weight loss, anorexia, dyspnea, and pulmonary infection. The subsequent course of the disease, however, was unpredictable from the initial favorable response to the treatment, and the duration of remissions was not always a result of treatment. In 4 of the 7 patients who showed improvement after treatment, the remission was maintained without therapy for a period of from 1½ to 3 years. No patient was cured either spontaneously or as a result of treatment. Five patients died; the death of 4 was attributed to berylliosis, and that of 1 to an unrelated disease. Four patients are sufficiently well to perform light housekeeping chores; 6 are partially disabled; in the remaining 4 the disease has been gradually progressive despite steroid therapy, adequate rest, limitation of physical activity, and other supportive measures.

Complications, such as hemoptysis, pneumothorax, and renal stones, were frequent in the series presented, but the development of cor pulmonale was the most serious threat and is now regarded as a poor prognostic sign. The chest roentgenograms showed characteristic changes in the early stage of the disease which are indicative of berylliosis. As the disease progresses, the findings become less specific, and the roentgenograms may lose all similarity to the original appearance.

The Pathologic Changes of Chronic Beryllium Disease. H. R. Dudley. A. M. A. Arch. Indust. Health 19:184-187 (Feb.) 1959 [Chicago].

The observations reported were derived from a review of 53 patients with chronic beryllium disease in the Beryllium Registry. The chronic reaction to beryllium compounds is similar in each organ involved. Whether directly introduced or vesselborne, beryllium compounds precipitate a lymphocytic, plasma-cell, and granulomatous reaction in the skin, liver, kidney, lymph nodes, and skeletal muscle. The myocardium, the spleen, and the pleura may be involved. The most important route of entry to beryllium into the body is by inhalation, and, since the beryllium compounds industrially used are poorly soluble, the lungs are the most frequently and seriously affected. The chronic active disease may yield to a chronic more indolent state; the transition is often marked by the development of fibrosis and of vesicular emphysema with persistence of lymphocytes. Pulmonary emboli are frequent, in addition to the occasional endarteritic changes seen in the involved lungs. Approximately 25% of the patients reviewed from the Beryllium Registry had small emboli in the peripheral vessels. Pulmonary emboli constitute a hazard for any debilitated patient, and they can be expected to increase in frequency if polycythemia, caused by chronic anoxia, is added to the disease pattern. Showers of small emboli from the veins of the extremities may produce exacerbation episodes in the respiratory difficulties of these patients.

Medical Aspects of Civil Jet Air Transport Operations. K. G. Bergin. J. Aviation Med. 30:22-28 (Jan.) 1959 [St. Paul].

This report covers the civil operation of Comet jet aircraft over a period of 8 years. With the exception of the intermission in flying after the misfortunes of some years ago, the experience covers

a wide range of operations over land and sea in tropical and temperate climates. A previously held conception that pilots for jet aircraft should be of the fighter pilot mentality has been proved to be misguided, and, by the same token, any arbitrary age limit of those competent to fly is not supported by experience. While reaction time may be slower in an older person, in the final analysis of reaction to conditions due weight must be given to the value of experience in any set of circumstances—the older and more experienced pilot carrying out his task with an economy of thought and action which is not available to his less experienced colleague. The pilot must be adaptable and prepared to adopt new techniques; he must be mentally alert; he must be more than usually ready to think and plan ahead; and, most important, he must be prepared to be a fully working crew member. Integrated teamwork on the flight deck is the key to successful jet operations. A pilot's reaction times must be swift, because he is working to a much shorter time scale, and his instrument flying must be exceptionally good, as instrumental approaches call for precision and accuracy. Careful preflight training and flight simulator work are important.

Jet aircraft and their flying technique do not require exceptional standards of physical or mental fitness. If anything, the danger is that their good flying characteristics could lead to a mistaken impression by nonflying executives that they are easier aircraft to fly than current piston-engine types. This view must not be allowed to gain credence. The operation of flight-time limitations, stacking at airports, fuel reserves, and the tiring effects of manual flying of such a sensitive aircraft, should the automatic pilot fail, must be given due consideration. The ideal pilot for operation of jet aircraft is one who is methodical and clear thinking, who has a mobile mind, and who fits in readily with a team. Good flight planning is required, and a high standard of training and indoctrination is most desirable.

THERAPEUTICS

Clinical Experiences with the Vitamin B_{12} Factors III and III$_m$ in the Treatment of Pernicious Anemia. G. Böwing and F. Thedering Jr. Blut 4:349-366 (Dec.) 1958 (In German) [Munich, Germany].

Numerous substances have been identified, which are chemically and biologically related to cyanocobalamin and which belong to the vitamin B_{12} group of substances. To classify the known vitamins of the B_{12} group, the authors survey the structure of the entire complex. A central cobalt atom is surrounded by 4 pyrrole rings, so that a porphyrin-like macro-ring system results. This system of rings contains 6 conjugated double-bonds. In the side-chains the basic ring is substituted with methyl groups, acetamide groups, and propionamide groups, and short and long side-chains are arranged in the same manner as in uroporphyrin III. One of the propionic acid chains, by way of an amide-bond, is connected with aminopropanol, the hydroxy group of which is esterified with the phosphoric acid rest of the nucleotide. In the chemistry of vitamin B_{12} a nucleotide is that portion of the vitamin B_{12} molecule that consists of an amidozole base, D-ribose, and phosphoric acid. A nitrogen atom of the base is connected with the cobalt atom like a secondary valence. This is important for the biological action. Depending on the groups coordinated with the cobalt atom, there are cyanocobalamin, hydroxycobalamin, nitrito-cobalamin, cyanato-cobalamin, thiocyanato-cobalamin, and others. A list of the complete nucleotide-containing "cobalamins" shows that factor III of vitamin B_{12} is hydroxybenzimidazole-cobalamin, and factor III$_m$ is 5-methoxybenzimidazole-cobalamin.

The authors discuss what parts of the B_{12} molecule determine its biological action, showing the relation between chemical constitution and biological effects. Of 14 patients with decompensated pernicious anemia, they treated 4 with factor III and 10 with factor III$_m$ of vitamin B_{12}. All achieved full clinical and hematological remissions. The effect on the blood picture, on the general condition, and on the spinal degeneration was the same as that of pure vitamin B_{12}, vitamin B_{12} plus folic acid, or liver extract. Primary treatment with the oral administration of factor III or factor III$_m$ plus intrinsic factor is possible, but treatment by injection is more reliable. Maintenance treatment by means of factors III and III$_m$ of 49 patients with compensated pernicious anemia achieved complete clinical and hematological control so far over an average period of 20 months. The patients reacted in the same way as they did earlier to treatment with liver extract, with vitamin B_{12}, or with vitamin B_{12} plus folic acid.

The oral administration of factors III and III$_m$ requires more careful supervision of the patient because of the danger of recurrence in this as in other oral forms of therapy. The dosage of factor III or factor III$_m$ is of about the same magnitude as that of vitamin B_{12}. Tolerance for factors III and III$_m$ was favorable; no undesirable side-effects were observed. The authors conclude that factors III and III$_m$ can be recommended for the treatment of patients with pernicious anemia.

Triamcinolone in the Treatment of Allergic Conditions. L. H. Criep. J. Allergy 30:50-60 (Jan.-Feb.) 1959 [St. Louis].

The author reports the results of treatment with triamcinolone (Aristocort) in 250 actively allergic patients (119 men and 131 women) of all ages. Many patients presented more than one type of

allergy, the duration of which varied from 1 to 10 years. The initial dose of triamcinolone was as follows: 206 patients received 16 mg. daily, 9 patients received 20 mg. daily, and 35 patients received 24 mg. daily. The dose of triamcinolone was reduced by 2 to 4 mg. a day every 1 or 2 days. The maintenance dose was 2 mg. daily in 155 patients. The drug was withdrawn gradually. No sodium-restricted diet or potassium was prescribed. The duration of treatment with triamcinolone ranged from 2 to 18 weeks. Usually other antiallergic treatment was continued during and after steroid medication, thus making it possible to employ smaller doses of triamcinolone.

Laboratory studies revealed no marked changes as a result of triamcinolone therapy in maintenance doses of 2 to 4 mg. daily. The hemoglobin level, hematocrit reading, and red blood cell count were unaffected. Eosinopenia occurred in 95 of 203 patients in whom the blood cell count was done. The chest roentgenogram was unaffected. In 4 patients glycosuria developed, and 5 patients showed a suggestive diabetic sugar-tolerance curve. No change in nonprotein nitrogen level was seen. There was no evidence of hypercalciuria or hypokalemia and no significant changes in total protein or gamma globulin values. Analysis of a metabolic study in 6 patients with bronchial asthma of long standing, who were given 18 to 24 mg. of triamcinolone, revealed only slight changes in urine sodium and calcium findings.

Triamcinolone is about 1½ times as potent as prednisone as an antiallergic agent and gives marked clinical relief. The frequency and severity of side-reactions are about the same as those observed with other synthetic steroids, except perhaps for fewer instances of hypertension and gastrointestinal manifestations. Most of the more serious side-effects occurred when the dose of the drug exceeded 10 mg. a day. Weakness, sweats, and muscle cramps were common side-effects found in this series. Sodium retention, potassium depletion, and edema were not observed after administration of triamcinolone in the dosages used. Triamcinolone commonly causes diuresis. A note of caution is included with reference to the use of triamcinolone and other steroids in the long-term treatment of allergy. Patients have to be examined regularly while taking the drug. Only the smallest dosage needed to keep a patient comfortable should be employed. Patients should be urged to be conservative in the use of the drug, and the possible dangers of long-term use should be explained to them. Most allergic patients do well with usual antiallergic therapy and do not need steroids.

Triamcinolone, as well as other corticosteroids, is indicated in the treatment of allergy only when it is used under the following conditions: (1) purely as a temporary measure in acute transient disorders, such as dermatitis due to poison ivy; (2) when it is impossible to control disabling manifestations, such as intractable bronchial asthma, in spite of complete medical and allergic treatment; (3) as a crutch during the period in which medical and allergic studies are being conducted if other forms of symptomatic therapy are inadequate; (4) in the absence of any of the well-known contraindications to steroids; and (5) as a lifesaving procedure in status asthmaticus. This therapy should be undertaken on a long-term basis only after a careful appraisal of potential dangers as well as benefits. It is not to be used as a substitute for careful medical and allergic treatment. Particular caution is to be exercised in the long-term treatment of allergic children.

Fluoxymesterone ("Halotestin") in Advanced Breast Carcinoma. B. A. Stoll. M. J. Australia 1:70-74 (Jan. 17) 1959 [Sydney].

The effects of fluoxymesterone (Halotestin) in a series of 50 patients with advanced cancer of the breast were studied at the Peter MacCollum Clinic, Melbourne. Fluoxymesterone was administered by the oral route in daily doses of from 15 to 20 mg. to less than one-half of the patients, and was given in daily doses of from 25 to 45 mg. to the remaining patients. Definite improvement was noted in patients with soft-tissue metastases to whom daily doses larger than 20 mg. were given. The response to the treatment was analyzed in 22 patients with cancer of the breast with metastases to the bone. Relief of pain was obtained in 18 patients (82%), and recalcification of metastases, without simultaneous roentgenotherapy, in 3; in 1 of the latter the recalcification of metastases was obtained after 6 weeks of treatment, and in the other 2 within 8 to 10 weeks of treatment. The duration of remissions effected in the majority of patients with metastatic breast cancer was 3 to 6 months only, but the favorable response was maintained for 9 months or longer in 3 patients. The results obtained with fluoxymesterone were similar to those observed from testosterone propionate.

Twenty-nine patients presented soft-tissue growth involving breast, lymph nodes, or cutaneous nodules; a favorable objective improvement was noted in 8 (27%), which was better than that observed from testosterone propionate. The best response was obtained in patients with primary growth, also in one patient with a recurrent tumor. The improvement has been maintained now for 6 months or longer in 3 patients, and they are still in remission although fluoxymesterone treatment has been discontinued. The 5 patients with pulmonary metastases showed no regression of lung opacities, and there was no reduction of the pleural effusion.

The urinary calcium levels were not in correlation with the clinical remissions: a fall in the urinary calcium excretion may occur (which is probably due to the calcium-retaining properties of fluoxy-

mesterone), with no concomitant clinical improvement. On the other hand, 2 patients with persisting high urinary calcium levels showed marked remission of symptoms. Side-effects were, in general, few. It is emphasized that the greatest advantage observed in fluoxymesterone therapy was that even the administration of clinically effective doses caused little or no masculinization.

Clinical Evaluation of a New Sulfonamide with Prolonged Action. G. Fontana. Minerva med. 49:4726-4730 (Dec. 15) 1958 (In Italian) [Turin, Italy].

Forty-one patients, male and female, 16 to 71 years of age, with various inflammatory diseases of the respiratory tract were treated with Orisul [3-(*p*-amino-benzolsulfonamido)-2-phenyl-pyrazol], a new sulfonamide preparation with prolonged action. Each patient received 2 Gm. of the drug the first day, and 1 Gm. per day from the second day on. The 2-Gm. daily dose was continued for a few days in patients with the severe form of the disease. Good results were obtained in 27 patients; the fever dropped within 24 to 48 hours and the values of erythrocyte sedimentation, leukocytes, and alpha$_2$ globulins became normal. Fair results were obtained in 9 patients; improvement followed from 5 to 7 days after the beginning of treatment. No results were obtained in 5 patients, who had to be treated later with antibiotics. Twelve of 15 patients with acute bronchitis improved rapidly; the symptoms regressed in the same manner as if antibiotics had been used. The drug had a less beneficial effect in 5 patients with subacute bronchitis or chronic bronchitis which had become acute. Fair results, though, were obtained in 3 of these patients and good results in 2; discharge of mucus and elevation of temperature improved after a few days of treatment. The substitution of Orisul in patients who had received penicillin caused no change in the course of their improvement. The drug had an effect similar to that of antibiotics in 15 patients whose bronchopulmonary diseases were not too severe, but substitution or integration therapy with antibiotics had to be used in other patients with the severe form of these diseases. The drug was well tolerated by all the patients.

Gastroduodenal Perforations and Prolonged Steroid Therapy in Lipid Nephrosis. J. Cathala, C. Polonovski and M. de Boissière. Presse méd. 67:41-43 (Jan. 10) 1959 (In French) [Paris].

The authors describe 2 cases of lipid nephrosis, one in a 14½-year-old boy and the other in a 2½-year-old boy, which ended fatally after the patients were treated with long courses of prednisone (delta cortisone). Autopsy showed that the cause of death was unquestionably related to the occurrence of duodenal and gastric perforation. The authors state that the usual treatment of lipid nephrosis includes a daily dose of prednisone until edema and albuminuria have disappeared and plasma disequilibrium is corrected. Then there is a maintenance period in which prednisone is taken 3 or 4 days of the week for several months. The posology of the drug is uncertain, and many believe that it is necessary to reach a certain dosage level of effectiveness. This leads to increasing doses in difficult cases up to amounts which far exceed what would ordinarily be used, considering the weight and age of the patient.

The 14½-year-old boy had a recurrent attack of nephrosis and was in danger of cerebral accidents and anasarca. Abdominal symptoms appeared to be in direct correlation with the bout of nephrosis. A decision to use prednisone was not without realization of the patient's intolerance to the drug and of the fact that his father had an ulcer. It was decided that steroid therapy was necessary, and corticotropin (ACTH) was substituted for prednisone. The patient died during the night after the new treatment was begun. Anatomic examination revealed punctiform purpuric spots in the gastroduodenal mucosa and a perforation of the duodenum. Histological examination revealed ulcerations of the duodenum and stomach, which were characteristic of ulcerations of prednisone origin.

In the second patient an attack of severe abdominal pain was treated as a nephrotic attack. Altogether this boy had received 920 mg. of prednisone over a period of 51 days, being given up to 50 mg. per day although he weighed only 12 or 13 kg. (between 27 and 29 lb.). After an apparent cure, he was hospitalized again and given potassium chloride, penicillin, and a French steroid preparation (Cortancyl) for grippe. Three days later he died, after an abdominal attack, of what seemed to be nephrosis and hematemesis, and in shock. Anatomic examination showed isolated perforation of the posterior wall of the stomach. In both this and the first patient the painful abdominal syndrome did not appear to be of a nature other than that of previous abdominal episodes. Circumstances were not favorable for a precise diagnosis or surgical intervention in either patient.

The cause of the nephrotic abdominal syndrome is infection in most cases, but other mechanisms may be at fault. Anatomic or functional disturbances in the adenomesenteric system or vena cava and changes in the protein-lipid equilibrium of the plasma can play a role. The difficulty lies in deciding whether an abdominal attack is the result of an infection in a patient with lipid nephrosis or whether it is a mechanical accident which may be the consequence of treatment. Steroid therapy risks causing lesions of the digestive mucous membrane, ranging from erosions and ulcerations to hemor-

rhagic necrosis and acute perforation of an organ. The question of treatment is very difficult, since steroid therapy is at present well accepted and it brings much success. The authors think that this therapy should be limited to less prolonged periods. The original basic and maintenance treatments, which could last for 6 to 8 months, might be more suitably limited to 3 or 4 months. Perhaps some abandoned methods which had some success (for example, thyroid opotherapy) could be used with a rigorous and prolonged antibiotherapy. This might improve the prognosis of nephrosis and avoid the definite risk of perforation from steroid therapy. The distressing problem of treatment for lipid nephrosis remains to be solved. This practical difficulty is the consequence of lack of knowledge of the nature and etiology of the disease.

Disseminated Lupus Erythematosus: Analysis of Cases of 100 Patients Treated with Corticosteroids: Comparison with 25 Untreated Patients. J. Jalil M., R. Armas Cruz, J. Harnecker J. and others. Rev. méd. Chile 86:717-732 (Dec.) 1958 (In Spanish) [Santiago].

One hundred twenty-five patients with disseminated lupus erythematosus were observed for at least 8 years in the hospital of the University of Chile in Santiago. Most of the patients were women. One hundred patients were treated with corticosteroids; 25 "controls," who were observed before the advent of corticosteroids, were treated with vitamins, analgesics, and colloidal gold sulfide. The incidence of clinical signs and symptoms, the laboratory findings, and the distribution of predominant lesions were approximately equal in both groups before treatment. Among the controls, 4 patients had 1 or 2 recurrences which lasted between 1 and 3 years. Four of the controls disappeared from observation; in the remaining 21 the disease followed a typical progressive, fulminant course. All these patients died within 2 months to 4 years from appearance of the symptoms (death rate of 100%). The main cause of death was lupus itself.

In the patients treated with corticosteroids, the time between appearance of symptoms and hospitalization varied between a few weeks in the acute cases and a few months in the chronic cases. Cortisone was given in an initial dosage of from 200 to 500 mg., followed by maintenance doses of between 6.25 and 12.5 mg. The maintenance therapy was sustained for a period of 1 to 8 years. Prolonged treatment resulted in improvement of the general symptoms, the joint pains, and the cutaneous lesions in 67, 81, and 72% of the cases respectively. All other symptoms of lupus either did not change or became worse. Thirty-three patients discontinued the treatment during an apparent cure or remission of the disease; 9 did not report for observation; 19 had recurrences between 1 month and 6½ years after discontinuation of the treatment; and 5 were still under observation, in an excellent condition, between 5 and 7 years after they had discontinued the treatment. By the end of 8 years, in the whole group of treated patients, 8 had discontinued the treatment, 50 with severe and moderately severe forms of the disease had died, and 42 are living and continuing the treatment. Of the 50 patients who died, survival between initial treatment and death varied between 2 months and 3 years in 22 patients with severe and moderately severe forms of the disease who had early, sufficient, and maintained treatment; it varied between 1 month and 4 years in 28 patients who had either late or insufficient treatment. The cause of death in these treated patients was lupus itself in 36% of the cases and intercurrent diseases in 64%. Forty of the 42 patients who have survived for more than 8 years are ambulant under minimal dosage of corticosteroids and carry on almost normal activity. Only 2 patients are invalids because of lupus. The authors conclude that corticosteroid treatment lowers the death rate from 100% in those not so treated to 54% in those treated. The earlier the start of the treatment, the better the results in prolonging survival with attenuated symptoms.

ANESTHESIA

Fluothane: A New Nonexplosive Volatile Anesthetic Agent: Preliminary Report on 2,000 Administrations. H. M. Ausherman and A. Adan. South. M. J. 52:46-52 (Jan.) 1959 [Birmingham, Ala.].

Fluothane (2-bromo-2-chloro-1, 1, 1-trifluoroethane), a clear volatile liquid which mixes well with oxygen and is not explosive or flammable, was given a trial as the principal anesthetic agent in 2,000 patients, between the ages of 5 weeks and 82 years, who were subjected to almost every type of surgical procedure. There were few poor-risk patients in this group. The length of operation in 66% of the patients was less than 2 hours. The semiclosed technique of administration utilizing the Copper Kettle, one of the most accurate vaporizers, was employed in 1,386 patients. Due to the ease with which one can administer a lethal concentration of this agent, the authors believe that a machine with such an accurately calibrated vaporizer is essential to the safe and proper use of this potent agent. The results obtained with this drug suggest that this halogenated ethane is of more than passing interest in filling the need for a controlled volatile nonexplosive anesthetic agent. The authors were impressed with the rapid smooth induction, the ease of maintenance with present equipment for anesthetization, the reduction of

salivation, the reversibility of the agent's action by controlling the vapor concentration, the adequate muscular relaxation for most surgical procedures, the rapid recovery time without excitement, the reduction in postoperative nausea and vomiting, and the minimal complications.

The commonest complication in administering Fluothane was too deep an anesthesia, especially with the use of the open-drop technique in children. Bradycardia occasionally occurred but usually was relieved by intravenous administration of atropine and by reducing the vapor concentration. Like cyclopropane, Fluothane increases cardiac irritability, and therefore drugs, such as epinephrine, should not be used with this agent. With Fluothane, vagal action on the heart predominates, perhaps explaining the slowing of the pulse, the lowering of the systolic blood pressure more than the diastolic resulting in reduced pulse pressure. The fall in blood pressure appears to be in direct proportion to the concentration of the vapor and especially to the rate at which the concentration is increased. Inhalation of Fluothane produces some degree of respiratory depression, but one of its desirable properties is the ease with which respiration can be controlled and spontaneous respiration be resumed when desired. In using the agent by the open-drop technique or by any method, the anesthetist must be alert and should be experienced. Properly used, it is one of the most useful anesthetic agents to date and deserves further study.

Fluothane: A Modern Substitute for Chloroform. H. R. Griffith, J. G. Robson, W. G. Cullen and D. M. M. Gillies. Anesth. & Analg. 37:316-321 (Nov.-Dec.) 1958 [Cleveland].

The authors' observations in the operating room and in the laboratory and a review of the literature convinced them that halothane (Fluothane) is a potent and versatile drug which may be used by preference in situations which demand a noncombustible controllable anesthetic agent. Halothane is not the harmless, foolproof drug that some of the anethesiologists have dreamed about as an agent to replace all explosive substances. However, it is somewhat less toxic than chloroform. Halothane is no drug for the amateur anesthesiologist. It should be administered in low concentration, with adequate oxygen and preferably some nitrous oxide as a vehicle, and adjustment of the concentration according to the patient's condition must be possible. Proper equipment is necessary for its relatively safe use, together with the most meticulous watchfulness, intelligence, and good judgment on the part of experienced anesthesiologists. Where these prerequisites prevail, halothane may acquire a most useful place in future anesthesiology.

Comparison of Meprobamate, Pentobarbital and Placebo as Preanesthetic Medication for Regional Procedures. E. I. Eger and H. H. Keasling. Anesthesiology 20:1-9 (Jan.-Feb.) 1959 [Philadelphia].

The authors carried out a double-blind comparative study of meprobamate, pentobarbital, and a placebo of lactose in 668 patients, between the ages of 16 and 96 years, who were to undergo surgical treatment in the University Hospitals or the Veterans Administration Hospital in Iowa City, for which a regional anesthetic was to be administered. Of the 668 patients, 199 were aged less than 60 years (young patients), 265 were over 60 years of age (older patients), and 204 were patients having some mild to severe mental impairment due to diseases of advancing age (senile patients). An attempt was made to determine the effect of each of the 3 preparations on the patient's apprehension, cooperation, drowsiness, reaction to painful stimuli, talkativeness, nausea, and emesis. The anesthetist's evaluation of the adequacy of each premedicant was also determined.

Either meprobamate or pentobarbital was more effective than placebo as premedicant in young patients, but this difference tended to become less in the older age group and to disappear in the senile group. In general, meprobamate or pentobarbital prevented an increase in apprehension, as viewed by either patient or anesthetist, this effect being most marked in the young patients, and absent or undiscernible in the senile group, while the older group may represent an intermediate between the other two. Cooperation was affected by meprobamate and pentobarbital in a significant manner only in the young patients in whom a decrease in cooperation was prevented. Sleep was significantly and favorably affected by the preceding administration of either meprobamate or pentobarbital as compared with placebo. Both meprobamate and pentobarbital caused an increase in drowsiness, the latter drug also causing a significantly greater degree than the former. No difference in the reaction to painful stimuli could be detected among the patients receiving either one of the two drugs. Talkativeness, emesis, and nausea were apparently unaffected by the drugs, although, in the case of nausea, increase in dosage was followed by decreased incidence; the effect of increasing the dose of placebo, however, was indistinguishable from the effect achieved by the increased dosage of the other drugs. Over all, the effect of meprobamate and pentobarbital is considered to be a favorable one and is most apparent in the group of young patients. No distinct advantage is seen in the use of one of the drugs as opposed to the other.

BOOK REVIEWS

Drinking and Intoxication: Selected Readings in Social Attitudes and Controls. Edited by Raymond G. McCarthy, Associate Professor, Health Education, Yale University, New Haven, Conn. Cloth. $7.50. Pp. 455, with illustrations. Publications Division: Yale Center of Alcohol Studies, New Haven, Conn.; Free Press, Glencoe, Ill., 1959.

Although this book is a symposium by 59 authors, expressing many viewpoints, the editor has successfully managed to present the problems of drinking, its complications, and possible remedies. After excellent chapters on the physiological and psychological effect of alcohol comes a most interesting discussion of the drinking habits of numerous cultures, from biblical times to the present. The illustrations are particularly well chosen and represent ancient statuary, bas-reliefs, and story-telling tapestries. Other chapters deal with the drinking habits of various ethnic groups, high school students, and college students, and contributory cultural, religious, and ethical factors. The account of the controversy between "wets" and "drys" is informative, and the motivation of the two groups is discussed in a logical manner. The reader will be particularly impressed, favorably or otherwise depending on his psychological background, with the chapter by Myerson, Alcoholism: The Role of Social Ambivalence. Hedonism, the worship and seeking of pleasure, is contrasted with asceticism, which runs counter to desire and satisfaction and when carried to its logical extreme is against reproduction: "Man is born into sin. He becomes a third excretion born between urine and feces." Man's ambivalence concerning sexual matters also applies to the use of alcohol. The author advises a middle course: "Against unwise hedonism, against extravagant asceticism, we need to build a code of temperate hedonism and successful self-control." The book should appeal particularly to the student of history, the sociologist, and the scientist. The worshipper of Bacchus may be persuaded to mend his ways, while the ascetic "dry" may feel that his convictions are not represented with sufficient vigor. Finally, this excellent symposium has succeeded in its purpose of furnishing knowledge, which will probably do more to control the improper use of alcohol than legislation alone.

Tumors of the Lungs and Mediastinum. By B. M. Fried, M.D., F.C.C.P., Associate Attending Physician, Montefiore Hospital, New York. Cloth. $13.50. Pp. 467, with 235 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1958.

This book, although not all-inclusive, presents most of the important data pertaining to tumors of the lungs and mediastinum. Much of this material is controversial, and the author has attempted to present the various theories clearly in an unbiased manner. Most of this study deals with bronchogenic cancer. An attempt was made to study, whenever possible, the incipient stages of this disease. This was done by obtaining records of previous hospital admissions and of private physicians who had treated the patients at an earlier period. This is no mean task. The second section is devoted to a study of tumors and cysts of the mediastinum. The frequency of these conditions is stressed as is the differential diagnosis between primary and metastatic lesions. Chapter 17, which discusses tumors of the thymus gland and thymic cysts, is especially good. The book is well illustrated with roentgenograms, photographs, line drawings, and photomicrographs. Bibliographic references are given at the end of each chapter. This book can be highly recommended.

Chemical Concepts of Psychosis: Proceedings of the Symposium on Chemical Concepts of Psychosis held at the Second International Congress of Psychiatry in Zurich, Switzerland, September 1 to 7, 1957. Edited by Max Rinkel, with Herman C. B. Denber. Cloth. $7.50. Pp. 485, with illustrations. McDowell, Obolensky, Inc., 219 E. 61st St., New York 21; George J. McLeod, Ltd., 73 Bathurst St., Toronto 2B, Canada, 1958.

This book is divided into (1) historical survey; (2) reports of chemical, clinical, and physiological studies on lysergic acid diethylamide (LSD-25), mescaline, epinephrine metabolites, chelation, serotonin, indole, and central and peripheral fluids; (3) neuroleptic patients; (4) genetic, biological, and philosophical considerations of schizophrenia; (5) surveys of theoretical and methodological aspects of the problem; and (6) a general appraisal by Gilbert Cant, the medicine editor of *Time*. It is pointed out that "Any illness, including mental illness, can be discussed in a variety of ways: chemical, biological, pharmacological, sociological, through to psychology, philosophy and religion, not to mention medicine and psychiatry"; that biological and chemical theories concern the present symposium; that current chemical theories chiefly envision endogenous toxic factors resulting either from imbalances of chemical substances normally occurring in the body or from the development of new substances; and that the new chemical approach arose from the observation of the psychotomimetic effects of a variety of drugs, particularly mescaline and LSD-25. An effort has been made to imitate mental disorders by the use of such drugs, to discover variable factors and controls, and so to unmask possible chemical bases for psychotic states. Most of the symposium is

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

devoted to a description of the behavioral effects of the chemical substances mentioned above in experiments on animals, as well as their subjective effects on normal and psychotic human subjects and to the theoretical interpretation of the results.

It is difficult to restrain one's enthusiasm for the chemical attack on the psychoses, as so vividly documented and brought up to date in this book. Weary with age-long discouragements in the therapy of the psychoses the physician eagerly embraces the possibility of a new understanding and a new and hopeful approach. Without question, the chemical concept of psychosis offers the most optimistic prospect in psychiatry today. One's enthusiasm is, however, like that experienced at the birth of a baby—directed to the promise of the future; for the accomplishments so far, while exciting, are only the first steps toward a distant goal. In the present volume much is said about chemical formulas and pharmacological theory, but there are, inevitably, uncertainties and often contradictions in detail, which eventually will be resolved. The fact that schizophrenic states are not convincingly imitated by any drugs used is recognized in this book, but there is scant appreciation that whatever schizophrenia is, it is not a single disease but a congeries of more or less related states. The promising chemical concepts of psychosis here outlined must be adapted to a more precise subdivision of symptomatology before precise formulations of chemical factors in mental illness can be made. Precision is even more necessary in attempts to modify, intensify, or diminish psychotic symptoms by chemical means in experimental work with human patients. Chemists working in this fertile field must be guided and informed by the best clinical skill in this delimitation of psychiatric categories. The medical reader will need to keep clearly in mind that while the so-called psychoses—chiefly schizophrenia and the affective psychoses—appear likely to be metabolic disorders, and so basically chemical, the neuroses are rather acquired ways of life, learned distortions of character, and unlikely to be vulnerable to chemical analysis. This book is highly recommended to every physician as presenting in easily intelligible terms the latest work in a promising field with tremendous implications for the future.

The Middle Ear. By Heinrich G. Kobrak. Contributors: J. E. Fournier and others. Foreword by John R. Lindsay. Cloth. $15. Pp. 254, with illustrations. University of Chicago Press, 5750 Ellis Ave., Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N. W. 1, England; University of Toronto Press, Toronto 5, Canada, 1959.

This book is timely, because the middle ear has assumed increasing importance in recent years as new operations have been devised to deal with the problem of hearing loss in both suppurative and nonsuppurative states. Untimely, however, was the sudden death of the author, in 1957, before the completion of this work. He had pioneered in demonstrating the acoustic vibrations of the eardrum and ossicular chain by means of stroboscopic cinematography. His "staging" of these highly successful films revealed him to be a master showman as well as an outstanding educator. Such observations and his knowledge of the subject in general form the basis of his contributions, mainly to the first part, discussing the middle ear in health and disease. Alvar Wilka and J. E. Fournier also contributed to this part. The second part deals with treatment. Dr. John R. Lindsay, who also wrote the foreword, discusses otosclerosis and fenestration; Dr. Samuel Rosen, the mobilization and fenestration of the stapes; Dr. Kobrak, the treatment of middle ear deafness by prosthesis; Dr. Horst Wullstein, tympanoplasty; and Dr. Fritz Zoellner, the plastic surgery of the sound conduction system of the middle ear.

To the extent that modern otology is dedicated to the elimination of conductive deafness this book provides a summary of the past and present knowledge of the subject; but the problems and failures in otosurgery are not sufficiently evaluated for the novice in this field of endeavor. The chapter on stimulus and function is excellent. As is so frequently the case in a work which represents a number of contributors an integrated assessment of each is lacking, but each person's current thought, which in this type of surgery is undergoing such rapid modification that tomorrow it may be outmoded, is coherently presented. The classification of the types of functional repair of middle ear lesions offered by Wullstein is valuable in understanding the problems involved. Zoellner's enthusiasm for the acoustic probe is not shared by all, but his warnings regarding the problems of achieving ideal results in closing the air-bone gap are much appreciated. Not enough emphasis is given to the adequate treatment of lesions before functional considerations. There is an excellent reference list for each chapter. Some of the black and white photographs and color plates leave much to be desired.

Physical Examination of the Surgical Patient. By J. Englebert Dunphy, M.D., F.A.C.S., Professor of Surgery, Harvard Medical School, Boston, and Thomas W. Botsford, M.D., F.A.C.S., Clinical Associate in Surgery, Harvard Medical School. Second edition. Cloth. $8. Pp. 375, with 203 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

This new edition of a comprehensive volume on the examination of the surgical patient emphasizes what the surgeon may learn by special attention to history-taking and a careful and knowledgeable elicitation of physical signs. The tools employed are the eyes, ears, fingers, and nose. Clear-cut illustrations portray the various conditions discussed in the text, and enough clinical information is given to

enable the reader to understand what a physical finding signifies. Every area of the body is covered except the eye, ear, nose, heart, and lungs, the authors believing that these areas are well presented in standard textbooks on physical diagnosis. That the surgeon is not relieved of careful examination in these fields is emphasized, since reliance on medical or other colleagues prevents personally knowing and evaluating all the data.

A perusal of all the information offered reveals a tremendous amount of material available to the reader, whether he be a student or practitioner; and even the teacher would do well to review this book. Several special chapters are particularly informative; these deal with examination of the head and neck, the abdomen of infants and children, the infected hand, the peripheral blood vessels, ulcer and gangrene of the extremities, examination for the detection of cancer, and the general principles and specific examinations of the traumatically injured patient. Such patients are encountered more and more in industry and transportation and are rightfully receiving greater attention.

It is true that laboratory tests and x-ray studies are providing much information about diseases and injuries, but fundamentally the beginning is the physician-patient relationship initiated by listening to what the patient has to say, asking searching questions, and making a careful and thorough examination. This book should be of immeasurable aid in maintaining a high standard of acumen in the time-honored skill of examining the patient.

Rapports présentés au III ème Congrès international d'allergologie, Paris, 1958. (Proceedings presented at the IIIrd International Congress of Allergology.) Edités par B. N. Halpern et A. Holtzer. [In French, English, German and Spanish.] Cloth. 6,000 francs. Pp. 940, with illustrations. Ernest Flammarion, 22 rue du Vaugirard, Paris 6e; Congrès international d'allergologie, 197 boulevard Saint-Germain, Paris, France, 1958.

In recent years the concept of allergy has begun to permeate many fields of medical research and clinical medicine, including infectious diseases, collagen disturbances, and autoimmune manifestations. These trends are reflected in this book. The symposiums presented deal with asthma, emphysema, the properties of allergic antibodies, recent advances in clinical allergology, the biochemical aspects of hypersensitivity (histamine, serotonin, acetylcholine, and slow-reacting substance), and autoimmune and isoimmune reactions (blood, encephalomyelitis, kidney, lupus and other collagen diseases, and homografts), atopic dermatitis, and allergic problems in different parts of the world. The contributors to this volume include Sir Henry Dale, Pasteur Vallery-Radot, Charles Loeffler, Peter Forsham, Elvin Kabat, Merrill Chase, Pierre Grabar, C. Jimenez-Diaz, Harry Alexander, Murray Peshkin, H. O. Schild, Richard Schayer, Bernard Halpern, W. D. M. Paton, Robert Good, W. J. Harrington, Max Samter, J. Dausset, P. Miescher, Guy Voisin, Marion Sulzberger, W. Jadassohn, R. L. Mayer, Bram Rose, William Sherman, and many others. Each brings his particular subject up to the minute. The result is that the book is an exposition of the status of clinical and experimental allergology more up to date and more detailed than any textbook. More than half of the articles are in English, while those in French, German, or Spanish have complete summaries in English. This volume should be profitable not only to allergists, but also to immunologists, internists, dermatologists, pediatricians, and progressive physicians in general.

Heart Disease in Infancy and Childhood. By John D. Keith, M.D., Assistant Professor of Pediatrics, University of Toronto Faculty of Medicine, Toronto, Richard D. Rowe, M.B., F.R.C.P., Clinical Teacher, Department of Pediatrics, University of Toronto Faculty of Medicine, and Peter Vlad, M.D., Instructor in Pediatrics, Department of Pediatrics, University of Buffalo School of Medicine, Buffalo. Cloth. $22.50. Pp. 877, with illustrations. The Macmillan Company, 60 Fifth Ave., New York 11; Brett-Macmillan Ltd., 25 Hollinger Rd., Toronto 16, Canada, 1958.

Seldom has a more satisfactory book appeared on this subject. It covers its field thoroughly and scientifically. It is voluminous yet both readable and conveniently organized for reference purposes. Its chapters are well arranged. Its writing is not dogmatic, and its bibliography is complete. The diagrams and photographs are instructive and illuminating. It should be in the library of every pediatrician and cardiologist, and should prove a useful reference to the general practitioner. This review is short because there is nothing controversial in the book. No single chapter or subject is selected for criticism or praise because they are all of equally high quality.

Practical Dermatology. By George M. Lewis, M.D., F.A.C.P., Professor of Clinical Medicine (Dermatology), Cornell University Medical College, New York. Second edition. Cloth. $8. Pp. 363, with 121 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

In the preface to this new edition the author states, "As expressed in the preface to the first edition, this book, designed as a text for medical students, a practical guide for general practitioners, and an aid in orientation for other specialists, was written to meet the often expressed desire of my students to have a concise and well-illustrated text which would still serve their needs after they enter practice. It seeks to describe, as succinctly as possible, the clinical features and the methods of management of the more common skin disorders. Emphasis throughout the text is centered on (a) means to accurate diagnosis and (b) selection of appropriate treatment. To the student and practitioner recognition and identification of skin lesions present the outstanding dermatologic problems, but therapy is often difficult and challenging."

All of these objectives have been successfully attained. The author does not claim to have produced an all-inclusive reference work, but the descriptions of the dermatoses are brief and accurate. The limitations of space do not permit controversial discussions of cause and treatment, and some of the author's colleagues may take exception to some of his statements concerning both. The photographs are excellent and are arranged in unusual groupings of four and six to a page with the legends below. The legends were difficult to follow because of lack of differentiation in the typography. This volume is a worthy successor to the first edition and certainly meets the desires of students to have a "concise and well-illustrated text which would still serve their needs after they enter practice." The publishers are to be congratulated on the excellent compositing of this volume.

Growth and Development of Children. By Ernest H. Watson, M.D., Professor, and George H. Lowrey, M.D., Associate Professor, Department of Pediatrics and Communicable Diseases, University of Michigan Medical School, Ann Arbor. Third edition. Cloth. $7.75. Pp. 334, with 75 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

This is the third edition of a text which was last edited in 1954 and reprinted in 1956. Since its original publication in 1952 it has become the "bible" for students and young pediatricians preparing for examinations by the American Board of Pediatrics. This edition retains much of the material of the previous ones, but changes and additions have been made in every chapter except the first. Many charts, tables, and graphs are included for summarizing purposes, but the authors are quick to point out that average figures thus arrived at may not apply to the individual. The entire chapter on the role of the endocrine glands has been rewritten, but unfortunately the publication date did not allow for the inclusion of recent interesting information about masculinization of the female fetus due to the administration of progesterones during gestation. The chapter on heredity and environmental factors is based on the assumption that there are 48 chromosomes in man. A footnote states that recent studies indicate that there are 23 pairs of chromosomes in man rather than 24 pairs as has been taught in the past, but the authors believe that in order to avoid confusion the old concept should be temporarily retained. Statistics in human heredity are still based on the old number of 48 and probably will continue to be for some time. The chapter entitled Behavioral Development has been changed to Behavior and Personality to emphasize the greater interest in the area of personality development. Over 100 new references have been added and it is apparent that a new edition of this excellent text is a worthwhile addition to recent literature on this subject.

Clinical Orthopaedics. Number Twelve: Fall, 1958. Anthony F. DePalma, editor-in-chief. With assistance of associate editors, Board of Advisory Editors, and Board of Corresponding Editors. Cloth. $7.50; $6 to sustaining members. Pp. 327, with illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1958.

This volume is similar in format to the preceding ones in the series. The first article, historical in nature and dealing with the life of Dr. Buckminster Brown, is interesting, and the series dealing with the lives of early orthopedists is well done. Too many of the younger orthopedists do not realize the importance of the contributions of the pioneers in their field, and these articles are an excellent historical review. The first portion of the book deals primarily with problems of disability evaluations and various rehabilitation programs and in general the scope, techniques, and conclusions are well founded. The fact that rehabilitation is a team effort is emphasized. The second section of the book is devoted to general orthopedics and contains many interesting articles. One is on whiplash injuries of the cervical spine. It is felt the term "whiplash" should be deleted as a diagnostic term and "cervical strain or sprain" be substituted. The last portion of the volume has a very interesting article in which the author correlates the changes in the skeleton of the gorilla with those in that of man. The last article, on the appearance of a sarcoma after a surgically treated fracture of the tibia, is a brief but interesting case report. In this excellent volume the photographs and roentgenograms are of high quality.

Staphylococcal Infections. By Ian Maclean Smith, M.D., Ch.B., F.R.F.P.S.G., Assistant Professor and Chief, Infectious Disease Division, Department of Internal Medicine, State University of Iowa, Iowa City. Paper. $4.25. Pp. 180, with illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

This is a brief, practical, working manual dealing primarily with the clinical manifestations of staphylococcic infection. The manner of presentation is simple and categorical. This has obvious advantages to the practitioner and to the reader who wants a gallery of thumbnail sketches of the infections caused by staphylococci, but the critical reader may wonder if matters are really so cut and dried. A brief résumé of the biology of Staphylococcus is followed by chapters on diseases of the skin, respiratory infections, osteomyelitis, the gastrointestinal system and abdomen, septicemia and endocarditis, miscellaneous problems, diseases of animals, and the treatment of staphylococcic diseases. This is a useful volume but it is not to be compared with such a scholarly work, for instance, as "Staphylococcus pyogenes and Its Relation to Disease," by Prof. Stephen D. Elek of London, which has simultaneously become available through the Williams and Wilkins Company of Baltimore.

QUESTIONS AND ANSWERS

PUBLIC WATER SUPPLY

TO THE EDITOR:—*Please comment on a community water supply on which the following report was made: actual hardness, 2.4 grains per gallon; compensated hardness (computed from actual hardness, iron content, and sodium content), 6.0 grains per gallon; iron, 1.8 ppm; sodium salts, 1.1 ppm; alkalinity, 2.8 (expressed in grains per gallon of $CaCo_3$); and suspended solids or turbidity, none. The acidity in the sample was caused by the presence of free carbon dioxide. It was estimated that the water sample as received contained about 100 ppm of free carbon dioxide. For an accurate determination of the carbon dioxide content, it is necessary to follow a special sampling procedure and to analyze for the carbon dioxide at the job site.*

R. F. DeWitt, M.D., Plymouth, N. H.

ANSWER.—The analysis indicates that the water corresponds in general to that from wells in the New England area. In hardness it is high for a soft water, and this is the case also for sodium salts and for alkalinity. The high iron content is undoubtedly of more significance than the hardness from the standpoint of the household or industrial use of the water. If troubles from the presence of iron in public water supplies are to be avoided, it is generally recommended that the iron content be no higher than 0.3 ppm. The iron in ground waters is due to the presence of this element in the earth's crust. The iron dissolves in ground water particularly when there is an excess of carbon dioxide and an absence of oxygen in the underground source. When a well taps this strata, the water, when first drawn, may be clear and colorless. After being in contact with the air, however, it loses its excess of carbon dioxide and the iron then tends to precipitate and form a brownish turbidity. When this water is used, the iron will collect as rusty stains on plumbing fixtures, glassware, laundry, and other articles with which it comes in contact. For this same reason the water is unsuitable for a number of industrial uses, including paper making, laundering, and dyeing. From the standpoint of human health, the water is not likely to be dangerous. When treatment plants are available for public water supplies, any excess iron can be removed by aeration, the use of coagulants, and filtration. Removal of minerals from water by ion exchange resins is also possible.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

POSSIBLE TUBERCULOSIS WITH LEUKEMIA

TO THE EDITOR:—*A 78-year-old man has had chronic lymphatic leukemia for years. His leukocyte count is now 30,000, with 60 to 70% lymphocytes. Two years ago nodules appeared in his neck and subsequently in his elbows and groin. The nodules were diagnosed by the pathologist as being malignant lymphosarcoma. These have responded well to x-ray therapy, the amount of irradiation required being small. Roentgenograms of the chest were consistently negative until in May, 1958, when a mass was noted in the right lung. A pathological fracture developed in the right clavicle. With the increasing spread of the lesion, a small dose of x-ray therapy was given to the right lung, producing a severe physical reaction. Sputum examined subsequently was said to contain tubercle bacilli on slide, culture, and animal inoculation. Bronchoscopy, four months later, gave the impression that the lesion was not tuberculous but neoplastic and not necessarily related to the leukemia. Sputum examinations, after the patient had been taking PAS and isoniazid, were reported by different laboratories as negative, as containing photochromogens, and as being positive for tubercle bacilli. Animal inoculation is now in progress. Should this patient be given a course of nitrogen mustard? There has been a weight gain of about a pound a week. Anemia (hemoglobin 8 Gm. per 100 ml.) has been corrected through cell mass transfusion. Physically, the patient appears well and is without fever or cough. Roentgenograms taken in August and December showed some extension of the mass. Should this patient be isolated, and what treatment is recommended?*

Virginia Downes, M.D., Milwaukee.

ANSWER.—It is not unusual for lymphocytic leukemia to pursue a benign course in persons beyond 65. The appearance of cervical, epitrochlear, and inguinal adenopathy is more probably related to the leukemia than to malignant lymphosarcoma, but it is difficult to differentiate histopathologically between these conditions. The good response to small doses of x-ray without subsequent reappearance of other nodes gives further support to this point. It was not stated whether there was a change in the hemoglobin or platelet level at this time.

The findings, however, of a lesion in the right lung associated with a pathological fracture of the right clavicle, do indicate a new process. While bone lesions are common in the leukemias, pathological fractures of the clavicle are rarely observed, particularly with chronic lymphocytic leukemia. The lesion spread rapidly between May and December, especially toward the end of this period.

It would be important to ascertain the amount of x-ray delivered to the pulmonary lesion (tumor dose) and whether the lesion responded favorably or not. The nature of the "severe physical reaction" was not stated. It would be essential to resolve the question of tuberculosis by smear, culture, and particularly guinea pig inoculation of the sputum and gastric contents. The right clavicular lesion should be examined by needle or open surgical biopsy. Needle biopsy of the lung lesion by bronchoscopy or a transthoracic approach should be made if the issue is still in doubt. Surgical thoracotomy should be considered only if the life expectancy warrants it.

The history suggests neoplasm of the right lung with metastasis to the right clavicle in a 78-year-old patient with chronic lymphocytic leukemia. If tuberculosis has added to the already complex situation the patient should be isolated. A bone marrow aspiration to ascertain the cause of the anemia should be obtained. Chlorambucil should be given if the lymphocytic infiltration is interfering with erythropoiesis. Corticoid supplementation may be helpful if increased hemolysis is present. Specific therapy to the right lung lesion should be deferred until the diagnosis is confirmed.

LOSS OF VISUAL ACCOMMODATION

To the Editor:—*A patient sustained a blow to his right eye while at work. Examination shortly after this injury revealed a visual acuity for each eye, uncorrected, of 20/20. The pupil of his right eye was fixed and dilated. The patient had a marked weakness of his right inferior oblique muscle, causing diplopia. Posterior segments and visual fields were normal, but he had a loss of accommodation in his right eye. After some time, the patient no longer noticed the diplopia, but a small amount, present on extreme left upper gaze, can be brought out under testing conditions. The patient still has a paralysis of accommodation, the near point of accommodation being 34 cm. in the right and 13 cm. in the left eye. The insurance company wants to know what percentage of visual loss he has.* *M.D., Illinois.*

Answer.—The 1955 official formulation of visual efficiency considers only four coordinating visual functions: (1) corrected acuity for distant and near vision, (2) visual fields, (3) ocular motility, and (4) binocular vision. Paresis of accommodation, aniseikonia, dominance, and depth of focus are among the ocular disturbances not included in the computation, as such disabilities have not yet been calculated on a scientific basis. Diplopia in the upper field is not considered significant unless present within 30 degrees of the center of fixation. The patient's visual disability depends on how important good depth perception is for the performance of his work. The near point of accommodation of his unaffected eye (13 cm.) corresponds roughly to that at the age of 33, while that of the affected eye (34 cm.) corresponds roughly to the age of 47. Hence, for binocular use of the eyes at 40 cm., he would require a near addition of 1.5 D. for the right eye only. This would produce a size difference in near vision of 2.5%, with the right eye having the larger image. General aniseikonia of this amount is probably within the limit of tolerance. If his affected eye is dominant, the visual disturbance is likely to be aggravated. The mydriasis lessens the depth of focus. With a pupil diameter of 3 mm., the depth of focus is 1.33 cm. at the reading distance and is reduced proportionately as the area of the pupil increases. In the absence of other criteria, the relative loss in the near visual acuity of the right eye is suggested as a basis for determining the percentage of visual loss. The visual acuity for near vision is usually the equivalent of 20/50 or 50% visual efficiency when 1.5 D. addition is required. Averaging the percentages of central visual efficiency for the right eye on this basis for distant and near vision gives 75% or a loss of 25% (Spaeth and others, *A. M. A. Arch. Ophth.* 54:462, 1955).

VISUALIZATION OF VASCULAR SYSTEM

To the Editor:—*Is there any material (preferably red) that can be injected into the blood vessels of a pathological specimen so that these vessels will stand out in contrast to any white substance such as brain tissue? The material should be something which will solidify after it has been injected. Cinnebar has been suggested, but this does not dissolve in water, and, therefore, it must be used as a suspension. Latex 571 has also been suggested, but I have no information as to how this might be used.*

W. V. Knoll, M.D., Brainerd, Minn.

Answer.—Older methods of visualizing the vascular system were performed with use of gelatin or agar colored with water-soluble dyes: red—basic fuchsin, eosin, borax carmine, water color vermillion, or congo red; and blue—methylene blue, nile blue, gentian violet, or methyl violet. These are injected in the melted state under pressures comparable to the blood pressure into the blood vessels of organs kept warm in a water bath. The agar is then "set" by immersion in a cold water bath. A review of these methods is given by Whitten (*Arch. Int. Med.* 42:846, 1928). Because gelatin and agar

are fragile and the dyes eventually diffuse into the surrounding tissues, latex or plastics colored with dyes soluble in organic solvents are used. These substances have the added advantage of permitting the tissues to be corroded away, leaving a bare mold of the injected vessels. Detailed description of the techniques and the sources of materials are given by Whitten (*Arch. Int. Med.* **42**:846, 1928), Smith and Henry (*J. Lab. & Clin. Med.* **30**:462, 1945), Narat and others (*Anat. Rec.* **64**:155, 1936), Batson and Bellet (*Am. Heart J.* **6**:206, 1930), Wolfe (*A. M. A. Arch. Path.* **61**:153, 1956), Bondurant and Smith (*Am. Rev. Tuberc.* **70**:570, 1954), and Liebow and others (*Bull. Internat. Assoc. M. Museums* **27**:116, 1947). Marcus and others (*A. M. A. Arch. Surg.* **74**:225, 1957) published beautiful color plates of cardiac blood vessels injected with a plastic but gave no references or description of the method. Vinyl and latex preparations, colored red, blue, and yellow, together with directions for use, can be purchased from Chicago Biological Supply House, 8200 S. Hoyne Ave., Chicago 20.

FLOW OF SPINAL FLUID

To the Editor:—*What difference, if any, is encountered in the size and number of drops per minute when 20, 22, or 24 gauge spinal needles are used, other conditions being equal, as in performing spinal taps on the same patient?*

R. J. Kent, M.D., Savannah, N. Y.

Answer.—If a liquid such as spinal fluid is allowed to drip from the pointed ends of needles of different gauges, smaller drops will be formed by the narrower needles. With use of 20, 22, and 24 gauge needles, the number of drops of water per cubic centimeter will be about 36, 42, and 60 respectively. During a spinal tap, however, fluid flows in the reverse direction and drops from the needle hub. Regardless of the bore of the needle, the hubs are of identical size, and the size of the drops will not vary. There will be about 15 drops per cubic centimeter. Actually, the size of the drop depends not on the lumen of the needle but on the available surface from which the drop is suspended before its weight makes it fall. The barrel of a large-bore needle offers more surface than the barrel of a fine-bore needle, and a needle hub offers much more available surface than either needle point.

If 20, 22, and 24 gauge needles of the same length are used for spinal taps, the size of the drops at the needle hub will be the same, but the number of drops that fall per minute will vary. A wide needle bore will offer less resistance to flow, and, other factors being equal, fluid will drop faster from large-caliber needles. The length of the needles and the pressure of the fluid being released are also factors. If the spinal fluid is under a pressure of 100 cm. H_2O and three-inch needles of 24, 22, and 20 gauge are used, one may expect (assuming no obstruction of the needle within the dura) 25, 68, and 130 drops per minute, respectively; 1.6, 4.5, and 10.1 cubic centimeters per minute, respectively; and 15 drops per cubic centimeter.

PERSISTENT CYSTITIS

To the Editor:—*A 70-year-old man was operated on for stones in the urinary bladder on Oct. 6, 1958. There were some inflammatory changes in the bladder due to the presence of stones. About 80 small stones were removed through a suprapubic incision, and a tube was placed in the bladder. The patient was given chloramphenicol and 1 Gm. of sulfisoxazole four times daily. After four weeks the urine was practically free of pus. On Nov. 8, a suprapubic prostatectomy was performed and a tube was again placed in the bladder. A balloon catheter was introduced through the urethra into the bladder and was removed 12 days after the operation. The tube through the incision was removed 10 days after the operation. Immediately after operation the patient was given tetracycline; later he was given erythromycin. When this therapy was discontinued sulfisoxazole was again given, but the urine continued to contain pus. A few shreds were present in each urine specimen. On Dec. 11, a urine culture was made and many Escherichia freundii, a Streptococcus faecalis, and Proteus rettgeri were isolated. The Esch. freundii were resistant to penicillin, streptomycin, tetracycline, and chloramphenicol but sensitive to nitrofurantoin; the Streptococcus was sensitive to tetracycline and chloramphenicol; and the Proteus was resistant to streptomycin, tetracycline, chloramphenicol, and nitrofurantoin. Urine culture on Dec. 19 showed a heavy growth of the coli-aerogenes group, nonhemolytic streptococci, and Staphylococcus pyogenes var. albus. These were resistant to streptomycin and the tetracyclines but highly sensitive to nitrofurantoin, methenamine mandelate, neomycin sulfate, and kanamycin. The patient drinks about eight glasses of water daily, urinates every two or three hours, and gets up twice at night. After urination is apparently complete, he passes a few drops of urine. What is the cause of this dribbling and the presence of shreds in the urine? Why can the patient not hold more than 6 oz. in his bladder? Please suggest appropriate treatment.*

D. J. Louis, M.D., Chicago.

Answer.—This man must have had an infected bladder to begin with. If he has diabetes, this should be controlled. The patient has done well considering that he has had two operations. His urinary volume will increase as soon as his infection is controlled. One must remember that this

man has had long-standing vesical neck obstruction in which time his sphincters have become impaired. This often will cause a patient to dribble. This consultant, therefore, recommends increasing the daily fluid intake to 3,000 cc., exercising the sphincter at the time of voiding, the use of proper therapy depending on bacterial sensitivity, and patience.

AUGMENTATION MASTOPLASTY

To the Editor:—*What is the current status of the use of plastic inserts to supplement meager breasts? Please comment on safety; percentage of good immediate and long-term results; consequences of failure; and preferred type of procedure.* *C. O. Murray, M.D., Crockett, Texas.*

Answer.—Augmentation mastoplasty as currently performed has not been accepted as a good procedure by most plastic surgeons. Theoretically, small breasts need bulk to fill them out. To do this, one should use some type of autogenous graft. A free fat graft from the buttocks should be the material of choice, but unfortunately fat transplants do not survive well. Some surgeons have buried plastic sponges beneath small breasts. While this material is relatively inert, it is still a foreign body. It produces some inflammatory foreign body reaction which makes the breasts become stony hard. In others, the reaction is so great that the material has to be removed. The surgical treatment of this complication may be difficult because of the fibrous tissue reaction that has developed. While no cases in human beings have been reported, it is known that these plastic materials can produce carcinoma in experimental animals.

PAROSMIA

To the Editor:—*A 17-year-old woman has always had a keen sense of smell. In the last two to three years odors have bothered her. In the past year a cafeteria was installed in the high school she attends, and the smell of cooking foods has nauseated her. This has become so severe recently that the smell of some foods has caused headache and severe nausea. She had marked tenderness over the duodenum. She was placed on an ulcer diet and the abdominal soreness improved. The smells have continued to nauseate her. The only other pertinent factors include hay fever and moderate nervousness. Can you suggest any further treatment?*

R. S. Srigley, M.D., Altus, Okla.

Answer.—Parosmia, or perverted sense of smell, if it is organic, is always cortical in origin. Thus, lesions of the uncinate gyrus or disease of the tip of the temporal lobe might produce a disagreeable olfactory sensation. These may be associated with seizures or constitute a seizure in the areas described previously. With this in mind, an electroencephalogram might be helpful in diagnosis. If the tracing demonstrates dysrhythmia in one or the other or both temporal lobes, investigation of the type of lesion would be important. If there is no tumor or other organic focal disorder, one would expect good results with anticonvulsant therapy. The physician should also be on the lookout for local nasal conditions such as empyema of the maxillary sinus and ozena from chronic atrophic rhinitis. These conditions should suggest consultation with a rhinologist. When the possibility of organic disease is ruled out, it is suggested that this patient might have hysterical parosmia. A careful psychiatric history should be of value. In hysteria, the whole function of the nose (as comprehended by the patient) is lost. If the situation is of psychic origin the answer is psychotherapy. It is difficult to see the connection between the duodenal tenderness and the parosmia.

PHOSPHATASE LEVELS

To the Editor:—*In a patient having 9.2 King-Armstrong units of acid phosphatase and 72 King-Armstrong units of alkaline phosphatase, is such an acid phosphatase level of any importance?*

Joseph Burns, M.D., Miami Beach, Fla.

Answer.—The exact interpretation of this rise in acid phosphatase level associated with a substantial elevation in alkaline phosphatase level is not possible without more clinical information, but the general principles underlying the interpretation of such results are outlined below. The determination of serum acid phosphatase level, that is, the phosphatase activity at pH 4.9, represents the activity of a distinct enzyme and not the residual activity at this pH of the alkaline phosphatase. In other words, it is possible to have alkaline phosphatase levels 40 to 50 times the normal value without having any increase in the acid phosphatase level.

The serum acid phosphatase determination performed with beta-glycerophosphate as the substrate rarely shows elevations in conditions other than carcinoma of the prostate. Such conditions as fecal impaction or prostatic massage may cause slight transitory elevations, but the King-Armstrong method in which phenylphosphate is used as substrate shows slight or moderate elevations in patients who do not have carcinoma of the prostate. Such elevations have been reported in patients with familial splenic anemia, metastatic carcinoma of the breast in women, Paget's disease, and various inflammatory diseases. In the patient mentioned, the elevated alkaline phosphatase level is undoubtedly due to an osteoblastic lesion or to an obstructive process in the liver. The moderate

elevation in acid phosphatase level (performed by the King-Armstrong method) may be due to any of the conditions listed above.

IRRITABILITY OF MYONEURAL JUNCTION

To the Editor:—*Recently, several patients have shown evidence of either increased irritability of the myoneural junction or primary muscle fiber hypertonicity in conjunction with such chronic states as sprains, myositis, poliomyelitis, or virus encephalomyelitis (Guillain-Barré syndrome). These patients, after such exertion as playing in a gym class, walking a little more than average, or using the previously involved muscles in physical activity, have what may be termed a "charley horse." What causes this condition? Quinine has been given in doses of 0.3 Gm. and has been successful in some but not in others. What is the best treatment?*

Earl F. Hoerner, M.D., Orange, N. J.

Answer.—No evidence exists in favor of increased irritability of the myoneural junction or of the muscle fibers in any of the conditions named. While the possibility of facilitation of reflex spasm of muscles exists in poliomyelitis and in virus encephalomyelitis by reason of involvement of internuncial neurons, this neurological explanation not only is speculative and not applicable to the other conditions mentioned but also is not of interest to the questioner. No muscular lesion is common to the group of conditions listed, but where muscle weakness is evident sprains occur much more easily. Similarly, when repair processes are incomplete after sprains or myositis, overactivity or trauma may easily lead to additional soft tissue injury and inflammation because of the susceptibility of the delicate vessels and fibers of the repair tissue. If this explanation is correct, proper support and a graduated program of activity would be indicated, and, empirically, this is successful. It is doubtful whether any drug would have any appreciable influence on this process. The trial of medicaments used to treat diseases involving overactivity of the myoneural junction, myotoma congenita, dystrophic myotonia, and paramyotonia probably would not be indicated.

BANKED BLOOD

To the Editor:—*May jaundice be caused by banked blood that has been processed for over 14 days? What is the maximum time processed blood may be stored before use for transfusion?*

Joseph T. Phillips Jr., M.D., Norton, Va.

Answer.—Whole blood drawn under recommended conditions into acid-citrate-dextrose solution and properly stored is clinically useful for 21 days after venesection. Deterioration of stored blood does occur, however. Such deterioration is minimal for the first 10 days of storage and then increases steadily. Deterioration is judged by the survival of erythrocytes after infusion into the recipient. Blood stored for 21 days has a 70% survival rate, i. e., 70% of the infused erythrocytes exhibit normal persistence in the recipient, while 30% are removed from his vascular system within 24 hours after infusion. It is these nonviable erythrocytes that provide hemoglobin and eventually bilirubin and, in some cases, jaundice. Such jaundice appears and disappears within 24 hours of infusion. The 21-day limit for bank blood storage is based on clinical study and experience as being tolerable.

Release of 20 Gm. of hemoglobin via nonviable erythrocytes is associated with an increase of 1 mg. per 100 ml. in serum bilirubin levels. Mollison estimated that 75 Gm. of hemoglobin would have to be released in vivo within an hour or two to produce clinical jaundice. The quantity of blood being infused and the basic health of the recipient must also be considered. The use of almost outdated donor blood should be avoided if possible, particularly in large amounts, in transfusing patients with known liver deficiencies. Such situations seldom arise, because most blood banks try to balance supply with demand so that blood will be used long before the expiration date.

OBESITY IN YOUNG BOY

To the Editor:—*A 12-year-old boy has sex infantilism with obesity (adiposogenital dystrophy). He has been given weekly injections of chorionic gonadotropin and 30 mg. of thyroid extract daily. He has continued to gain weight despite a rather limited diet, and the genitalia are still immature and show no evidence of normal growth. He has recently been given 5 mg. of methyltestosterone twice daily. What further treatment is recommended?* *C. W. May, M.D., Tacoma, Wash.*

Answer.—With the patient only 12 years of age, one would be skeptical of the diagnosis of adiposogenital dystrophy in the absence of clinical and/or laboratory evidence of an intracranial tumor, cyst, or injury or previous encephalitis. His obesity may have no relationship to this syndrome but may be exogenous due to excessive eating; furthermore, the small genitalia may be relative, due to an abundance of fat in the pubic region. Small genitalia before puberty may be physiological. If treatment is indicated, chorionic gonadotropin may be given in doses of 1,000 I.U. three times weekly for six weeks, followed by 5 mg. of methyltestosterone twice daily for six weeks, with these drugs alternated for several months according to the clinical response. In addition, the calorie intake should be controlled by a diet with 1,000 to 1,250 calories daily. It may be necessary to evaluate emotional factors and correct these if possible. If weight cannot be reduced by diet alone, an appetite depressant may be needed, such as 10 to 15 mg. of pro-

longed-action dextro amphetamine sulfate given once daily after breakfast. Unless this boy has evidence of hypometabolism, there is no indication for the administration of dessicated thyroid. Failure of response to this regimen by the time puberty should appear (13 to 14 years of age) warrants a thorough endocrinological investigation.

RECURRENT CARBUNCLES

To the Editor:—*A 35-year-old woman has had six separate episodes of skin infection, usually large carbuncles, during a nine-month period. Each lesion was located in a different part of the body, usually above her eyes or on her arms. Culture on one occasion revealed Staphylococcus pyogenes var. aureus, which responded each time to erythromycin. All lesions required incision and drainage but cleared with the usual treatment and without complications. The patient's brother has diabetes but her own urine was negative for sugar on numerous tests. Use of hexachlorophene soap has been tried for short periods but not continuously. What would be the best prophylaxis against further skin infections?*

M.D., Utah.

Answer.—In such cases long continued prophylactic measures are required. This means a constant effort should be made to maintain a state approaching surgical cleanliness of the entire skin surface. There should be a brief bath every night with hexachlorophene soap. After this the skin should be dried, and then 70% ethyl or isopropyl alcohol should be applied to the entire body surface. For maximum protection, the alcohol may be applied night and morning. If this leaves the skin too dry, a bland oil may be applied afterward. The patient must be cautioned against fingering or picking at the skin, because infection is often conveyed in this manner. The towels, underwear, nightwear, and bed-linen should be boiled whenever they are laundered. An autogenous vaccine might be helpful, but one should not place too much reliance on this. In view of the family history, an occasional blood sugar estimation would seem advisable. For the treatment of active lesions, the erythromycin would appear to be satisfactory.

PAINFUL LAVAGE OF EXTERNAL AUDITORY CANAL

To the Editor:—*Why do some patients experience severe pain with lavage of the external auditory canal?*

Clinton F. Carrougher, M.D., Brooklyn, N. Y.

Answer.—It is assumed that the pain referred to was associated with attempts to remove impacted cerumen. This may occur because the skin of the external auditory canal is extremely sensitive to pain and, in some instances, impacted cerumen is hard and almost calcareous in composition so that, when it begins to move out of the external auditory canal with lavage, it acts as an abrasive on this sensitive area. Again, if the wax is hard and lies beyond the isthmus of the external auditory canal, its passage through the isthmus may produce a great deal of pressure against the skin in the isthmus and cause pain.

PERSISTENT PYURIA

To the Editor:—*A patient with a chronic urinary infection has been unresponsive to treatment with sulfisoxazole, nitrofurantoin, and chloramphenicol on separate occasions. Culture of the urine showed a gram-negative rod, probably a Proteus, although the exact organism was not identified. Sensitivity studies revealed resistance to all antibiotics tested. The patient is asymptomatic, but the urine shows a marked pyuria. What treatment should be given?*

A. F. Stratton Jr., M.D., Cocoa, Fla.

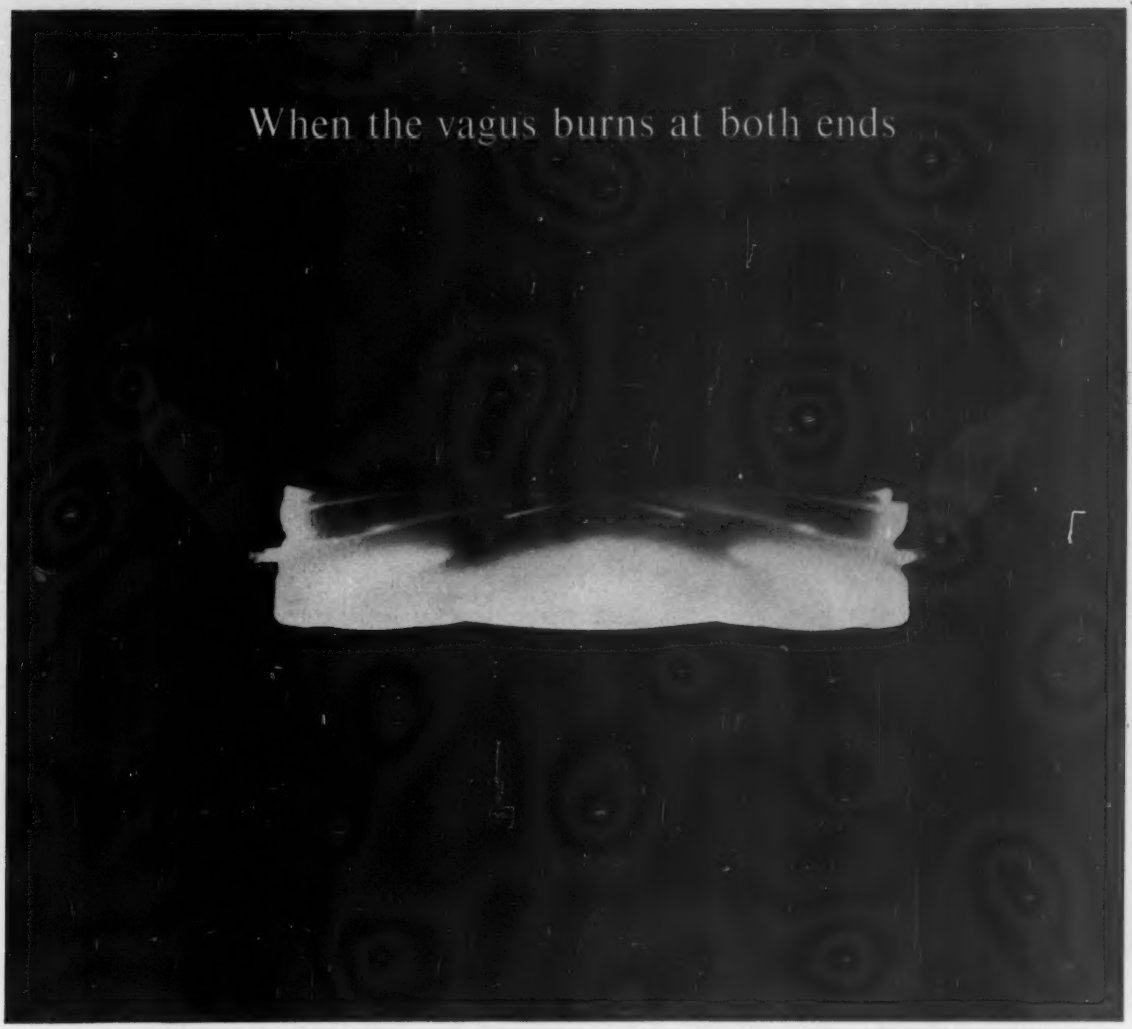
Answer.—Since the organism in this infection has not been identified, it would be difficult to suggest what antibacterial agent might be most effective. If sensitivity studies did not include kanamycin, this drug should be considered and sensitivity tests made. It is effective against some types of Proteus, all other gram-negative bacilli except Pseudomonas, and all common coccic bacteria except enterococci. Kanamycin is administered, preferably, in a dosage of 0.5 Gm. intramuscularly every 12 hours for six days, although many infections will respond to 1 Gm. given intramuscularly every 24 hours for six days.

MEASUREMENT OF REACTION TIME

To the Editor:—*What are the most practical clinical methods and equipment for the measurement of reaction time, where job safety demands average or above average general alertness? Does the measurement of the reaction time of the ankle jerk have any special validity for this purpose?*

Philip A. Fuqua, M.D., Richland, Wash.

Answer.—The ankle jerk reflex time would have no value as a measure of a person's ability to respond in complex job situations. In the latter motivation, attention and accuracy of judgment are more important than simple measurements of the time required for nerve impulses to travel to and from the spinal cord. A simple visual motor reaction time measurement is described by Schwab (*Neurology* 8:719, 1958). More complex reaction time tests requiring discrimination between signals may be of more value. The advice of a psychologist trained in these methods may be of value in devising tests applicable to the job situation at hand.



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References: 1. Charles, C. M.: Geriatrics *2*:110 (March) 1956. 2. Menger, H. C.: Clin. Med. *4*:313 (March) 1957. 3. Shuster, B. H.: M. Clin. North America *40*:1787 (Nov.) 1956.

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The A. M. A. offers placement assistance through the Physicians Placement Service, Council on Medical Service, 535 N. Dearborn, Chicago 10. This service is for the use of physicians seeking a location, as well as physicians seeking an assistant or associate.

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EUROPEAN MOTORING MANUAL—POCKET SIZE complete information; trip preparation and maps; data on 15 countries; motels, hotels, restaurants; shopping, kilometer charts; road and route data. Send $2.00 for postpaid copy to: E. S. Lee, P. O. Box 5505, Daytona Beach 14, Florida.

PRECEPTORSHIP IN SURGERY IN VETERAN'S ADministration Hospital in Arizona; available approximately July 1, 1959; require recent completion approved three or four residency; initial stipend $9,890, per year. Box 8056, % AMA.

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INTERNIST—OR GENERAL PRACTITIONER WITH interest in internal medicine, for position of staff physician in new, completely equipped 250 bed general hospital in West Texas; pleasant climate all year round; excellent retirement plan, life insurance, annual leave, sick leave and other benefits; salary from $9,890 to $12,770 depending on qualifications, with regular increases to $13,970 plus 15 percent specialty allowance to maximum of $16,000 if Board Certified. Apply: Personnel Officer, Veterans Administration Hospital, Big Spring, Texas C

(Continued on next page)

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TONICS AND SEDATIVES

• • •

My Favorite Story

In this space will be published anecdotes submitted by physicians concerning their practice or people in general. Contributions for "My Favorite Story" are welcome.

This story concerns World War II, when the heir of a wealthy family was serving as a petty officer on a submarine. The captain, who was exceedingly economy minded, repeatedly warned the crew, "Torpedoes are expensive. Before you release one, make sure you're going to hit the target."

Some days later the wealthy officer spotted a destroyer headed toward the submarine. "Destroyer on port side," he shouted into the megaphone.

No answer.

"Destroyer 400 yards away," he shouted.

Again no answer.

"Two hundred yards away!"

No answer and no action.

"One hundred yards away!"

Nothing.

"Fifty yards!"

Still nothing.

"Fire!" shouted the officer, "I'll pay for it."

The following conversation was overheard in an automobile showroom. "How's business?" the proprietor was asked.

"To tell the truth, it could be better."

"How's that?"

"It's those small foreign cars. They have really made an impression. The city is so full of them that whenever you cross the street, you not only have to look right and left but down."

•

A funeral procession was wending its way to the cemetery. The partner of the deceased gentleman was following behind the hearse. Just before they reached their destination, a big coal truck pulled out from a side road into the opening between the hearse and the first car.

On seeing the coal truck in front of him, the friend said, "I knew where Henry was going, but I didn't think he had to furnish his own coal."

(Continued on page 212)

(Continued from preceding page)

The Medical Bureau

900 North Michigan Avenue Chicago

ADMINISTRATION: (AA16) Dir 2 hosps, combined capacity over 1000 beds; fully approved, all specialties; med school affil; JCAH; W.
ANESTHESIOLOGY: (B66) Dir dept, new 170-bed hosp recently built at cost of 4½ million; fee-for-service which should net $15-$20,000 1st yr; coll town 100,-000, W.
DERMATOLOGY: (D58) Ass'n, 14-man group, all cert or elig; expan prog, oppor partnership; city 75,000, So. Calif.
GENERAL PRACTICE: (F53) With special int in OB; small group; liberal starting sal, partner within yr; modern bldg; coll town 15,000, Calif. (F54) Ass'n, 4-man group with own hosp; early partnership; small city, NE Texas. (F55) Ass'n, another GP; if capable gen surg, $1100-$1400 mo., with oppor %; well equip. clinic, nr Seattle.
INDUSTRIAL MEDICINE: (C17) Med dir, to estab medical prog, new plant; excell oppor; city of 120,000, SE Texas.
INSURANCE MEDICINE: (K54) Chief med officers, NY & MW offices, major co; internists or GPs.
INTERNAL MEDICINE: (K29) Cert or elig; 19-man group, long estab, in city 20,000, central Calif. (K30) To head dept, 50-bed community hosp, nr Chicago; $12-$15,000, plus % of priv. pract. (K31) Gastroenterologist; ass'n 3 internists; pract limited to int med & sub-specialties; new bldg; salary, followed by %; 90 min. driving time, NYC.
OBSTETRICS-GYNECOLOGY: (J77) Ass'n, 4-man group; res. town, 40 miles from NYC. (J78) Ass'n, cert obgyn; salary start, with partnership oppor; Chicago.
ORTHROPEDICS: (K13) 17-man group needs 2nd orthop, cert or elig; So. Calif. (K14) Ass'n 2 orthop, both cert & on faculty med school; salary or priv pract 1st yr, then full partnership; South.
OALR: (E65) Oph., cert or elig; growing clinic, one of largest towns, Alaska; $14,000 1st yr, $16,000 2nd, $18,000 or more, 3d.
PATHOLOGY: (L29) Dir dept, 200-bed fully approved hosp; coll town, 70,000, South. (L30) Ass'n, 2 Board paths; pref int clinical path; will spend majority of time at outstanding hosp, delightfully located on Coast; Calif; min $20,000.
PEDIATRICS: (M42) Ass'n, 2 cert ped, with univ. research & hosp assoc; partnership within yr; city of 300,000, many educ institutions; East.
P & N: (P48) Med dir, mental health clinic, univ city 120,000, MW; $9000 for half-time, good oppor for priv pract.
RADIOLOGY: (R78) Ass'n, 2 Board men; $15,000 1st yr, then %, $30,000; NY State.
SURGERY: (U60) 25-man group; pref. with thoracic & cardiac training; city, million pop., 2 med. schools, E.
UROLOGY: (W51) 10-man group; oppor teaching & research; univ city, 800,000, South.

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GENERAL SURGEON—BOARD ELIGIBLE OR BOARD Certified preferred; at new, completely equipped 250 bed general hospital in west Texas; pleasant climate; excellent retirement plan, life insurance, annual leave, sick leave and other benefits; salary from $9,890 to $12,770 depending on qualifications, with regular increases to $13,970, plus 15 percent specialty allowance to maximum of $16,000 if Board Certified. Apply: Personnel Officer, Veterans Administration Hospital, Big Spring, Texas. C

ASSISTANT DIRECTOR OF ANESTHESIOLOGY — Position open 500 bed charity hospital; new building to be occupied January, 1960, well equipped, ten operating rooms; excellent training programs in all specialties, twenty interns; thirty-five residents; teaching program supervised by Board Certified physicians on staff; eligible for Board Certification, California license required; salary $1,096-$1,332; good climate; rapidly growing community. Contact: Medical Director, Santa Clara County Hospital, San Jose, California. C

EPIDEMIOLOGIST, MD FOR POSITION IN LOS ANgeles County Health Department to act as advisor and consultant to Air Pollution Control District and other agencies combating smog; must have 3 years experience in diagnosis and control of communicable diseases of which one year in public health work. Apply: Los Angeles County Civil Service Commission, 501 N. Main Street, Los Angeles 12, California, telephone Madison 9-3521. C

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(Continued on page 212)

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The Poetry Corner

There was a Young Lady whose chin,
Resembled the point of a pin;
So she had it made sharp, and purchased
a harp,
And played several tunes with her chin.

•

The Children's Hour

The best and most original humor often comes from the remarks of children and their interpretations of everyday problems of living. Some examples are as follows:

A third grade teacher asked her pupils to draw a picture of what they wanted to be when they grew up. The pictures came in—nurses, firemen, spacemen, engineers, etc. But one little girl handed in a blank sheet of paper.

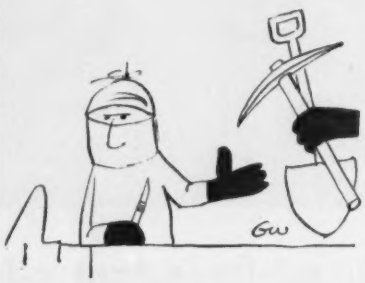
"Don't you know what you want to be when you grow up?" asked the teacher.

"Sure, I know," was the answer. "I want to be married, but I don't know how to draw it."

•

A mother and her small son were shopping for shirts in a department store. The mother had selected a bright red shirt for the boy. He evidently wasn't interested. "Why don't you like the shirt?" his mother asked.

"Because," he said, "it won't show the blood."



One young man, in his first year at boarding school, wrote to his folks air mail special delivery. His letter said, "Send food packages. All they serve here is breakfast, lunch, and dinner."

•

A little girl was having dinner at her friend's home. Buttered parsnips were being served. Her friend's mother asked if she liked them.

"Oh, yes," said the child.

"But," said the mother, "you're not eating them."

"Oh, I like them," was the answer, "but not well enough to eat them."

•

Quotes of the Week

If you don't think women are explosive, just try dropping one.

(Continued on page 214)

(Continued from page 210)

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DERMATOLOGY: (a) Assn w/22 Dipl grp (2 derms); well-estabd, excel facils; serv 300 bd, fully-apprvd hsp; serves 100-mi. radius; MW.
FOREIGN: (d) Hsp & ofc pract; 2 yr contract; about $12,000; transportation; Pacific Island.
GENERAL PRACTICE: (o) One exper'd & capable surg; join excl ol grp; $1,100-$1,400 mo, increases every 6 mos, % 3rd yr; 4 wks vac yrly; PacNW. (p) Assn 7 Bd specialists, 5 GP's; expansion prog; if well-qual'd, $15,000 w/oppor immed prtnrshp, no investmt; 3 wks vac, 2 wks study time, pd; MidE.
INDUSTRIAL MEDICINE: (o) Med Dir, lge rubber plant; jointly-owned, 2 impor co's; comprehensive med prog; good facils; excel sal & benefits; SW.
INTERNAL MEDICINE: (g) Old, est'd private prtnrshp, 5 man, 100 bd hsp grp, expndg; bldg new clinic; lge OPD; substantial guar til estbd; SE. (h) Bd elig; one seek's assn w/Bd Internist; nr Santa Barbara, California.
OALR: (y) Oph; Dipl; new post; hd dept; 11 man grp; $15,000, increase % each yr; prtnr 5th yr; PacNW. (z) Hd dept; 7 man grp (4 Dipls); sal plus %; early prtnrshp; univ city, SE.
OB-GYN: (a) Asst Dipl, Obgyn; 9 Dipl grp; 100-bd hsp, expndg; $12-14,000; SE. (f) Hd dept; new post; 3 man specialist grp—expndg; new bldg, fully-equip'd; share income & expenses equally; no initial investmt; nr San Francisco.
ORTHOPEDICS: (d) Assn w/Bd orthoped, FACS; lge amt referred wk; now grossing $100,000; $18,000 1st yr, then %, increase to 50%; Carolinas.
PATHOLOGY: (f) Hd dept, 100 bd hsp expndg to 200 bds; possibly serv 2 sml nrby hsps; financial arrngmts open; Mideast. (g) Bd Elig; capable assume Dept head, few yrs; JCAH hsp expndg to 300 bds; sal open; city 125,000, SE.
PEDIATRICS: (i) Assn, Bd ped; estd 10 yrs; $16,000 1st yr, then %; prtnr; vic Detroit.
P & N: (e) Psy; hd dept; new post; 13 man grp, mostly Dipls; oppor prtnr, 1 yr; 50% collections 1st yr, 55%, 2nd; famous resort area, Fla. (f) Neuro; assn w/Dipl, neurosurg, FACS, asst prof, affilns w/6 excel hsps; sal open—all fees from neuro cases, diagnostic tests—shld net $20,000, short time; univ city E.
RADIOLOGY: (d) Assoc w/2 Dipls, Rad; all modern equipmt; 500 bd, fully-apprvd hsp; $25,000 guar, 1st yr, lead'g to full-prtnrshp; SE.
SURGERY: (h) Well-trnd; under 35; assn w/surg, well-estbd; $15,000 plus %; early prtnr; NW.
UROLOGY: (v) Assn ol grp, 18 Bd or Bd elig men, estabd '39; $15,000; city 100,000, Midwest.

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WANTED—PSYCHIATRIST; DIRECTOR OF COMMUnity mental health clinic; diplomate or Board Eligible, licensed in New York State; experienced, well trained, full time psychiatric social worker; one half-time psychiatric social worker, and psychologist on the staff; five full days per week; salary open; needed immediately. Give full qualifications to: Box 573, Olean, New York. C

WANTED — BOARD CERTIFIED INTERNIST: FOR full time hospital practice in professional care program of the Miners Memorial Hospital; experience in the field of hematology preferred; starting compensation $18,000; progressive pay scale. For details address: The Clinical Director, Miners Memorial Hospital Association, 1427 Eye Street, N. W., Washington 5, D. C. C

PHYSICIANS FOR ADMITTING AND EMERGENCY ward for a large university and teaching hospital; excellent experience for physician interested in a university hospital; good salary and liberal fringe benefits. Please direct inquiries to: Administrator, H. N. Hooper, Cincinnati General Hospital, 3231 Burnet Avenue, enclosing a copy of your credentials. C

SOUTHERN CALIFORNIA GROUP OF 14 SPECIALists wishes to add the following certified or eligible men: orthopedic surgeon; ophthalmologist; ENT or EENT man; dermatologist; urologist; neurologist; and internist with allergy interest; these positions would lead to subsequent partnership status. Write: Administrator, Box 126, Downey, California. C

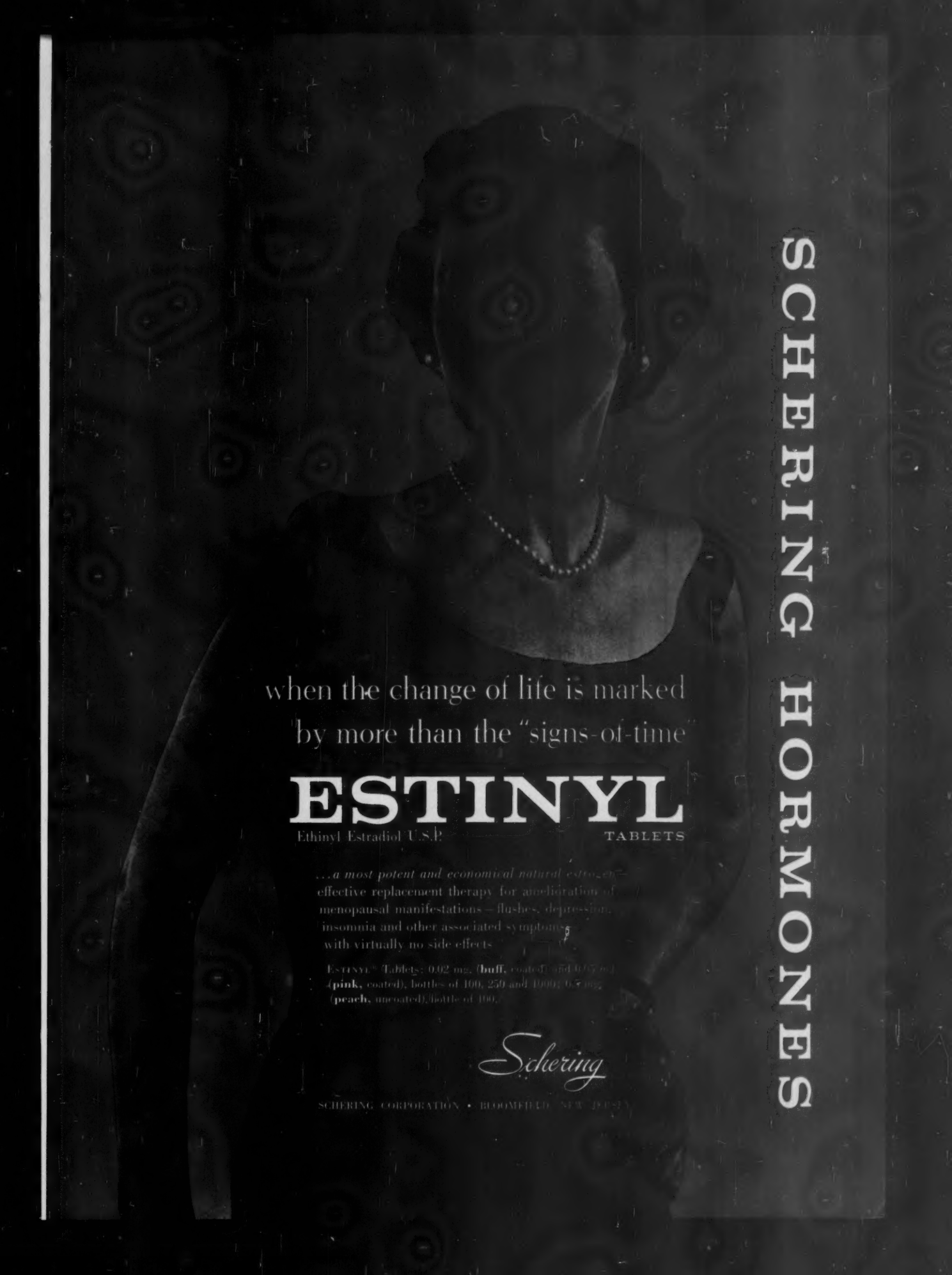
WANTED—GENERAL PRACTITIONER FOR COMMUnity in northern Wisconsin recreational area; practice established twenty-five years; doctor retiring; no doctor within twenty miles; large home and office combined for sale or rent with or without office equipment; terms arranged. Write: Ogema Lions Club, Ogema, Wisconsin. C

FAMILY PHYSICIANS — IMMEDIATE OPENINGS with medical group, southwestern Pennsylvania; excellent educational opportunities; paid annual vacation and study period; net starting income $12,000-$17,000 depending on training and experience; no investment required. Write: Box 8050 C, % AMA.

NEUROLOGIST—BOARD CERTIFIED OR QUALIFIED; required to assist in training and supervision or residents in active teaching hospital, answer consultations, participate in clinical conferences; opportunity for research. Write: Director, Professional Services, Veterans Administration Hospital, Bronx 68, New York. C

NEUROSURGEON NEEDS NEUROLOGIST FOR CITY serving 250,000 people with 1,000 hospital beds; excellent research facilities available. Box 8026 C, % AMA.

(Continued on page 241)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Liverwurst sausage

for iron *and* vitamins*

and good taste, too!

Doctors will be interested in the laboratory report based on the analysis of this KOSHER-ZION PURE BEEF LIVERwurst SAUSAGE . . . Children and Adults will like the *flavor* of this tasty way to eat 100% PURE BEEF LIVER. It is a pleasant way to encourage children particularly, to consume significant amounts of Iron, Phosphorous, Riboflavin, Vitamin B-12, Vitamin A plus other essential vitamins and minerals.

**Each 100 grams (approximately 3½ ounces) of* KOSHER-ZION PURE BEEF LIVERwurst SAUSAGE *contains:*

IRON	6.56 Milligrams
VITAMIN B-12	20.0 Micrograms
VITAMIN A	6,560 U.S.P. Units
THIAMINE	0.166 Milligrams
RIBOFLAVIN	1.80 Milligrams
NIACIN	5.67 Milligrams
VITAMIN C	13.0 Milligrams
PHOSPHOROUS	168.0 Milligrams
CALCIUM	37.7 Milligrams

**Report on Analysis by Laboratory of Vitamin Technology, Inc.*

KOSHER ZION BEEF LIVERwurst Sausage is of the purest, highest quality. It is not to be compared with other types of liver sausage that are processed for general commercial distribution. K-Z Beef Liverwurst Sausage can be purchased in popular sized packages sealed in saran casing for purity and preservation of freshness, at food shops, delicatessens and super-markets. It is reasonably priced.

KOSHER ZION SAUSAGE COMPANY
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TONICS AND SEDATIVES *(Continued)*

Girls are always running through his mind—they don't dare walk.

•

Nothing is impossible to the man who doesn't have to do it himself.

•

He is the kind of man who goes through life pushing doors marked "pull."

•

On her first visit to the doctor she gave him a preamble to her constitution.

•

Those who say "you can't take it with you" haven't seen a car packed for a vacation trip.

•

Anecdotes

An attractive young lady was standing in a hotel lobby obviously waiting for someone. A middle aged roué walked up to her, smiled, and said "Where have you been all my life?"

The girl looked him up and down and said, "Well, for the first half of it I wasn't even born."

•

They tell the story about a cannibal who loved his fellow men—medium rare.

•

They also tell about a man who was so rich that he served mixed greens for lunch —shredded $5's and $10's.

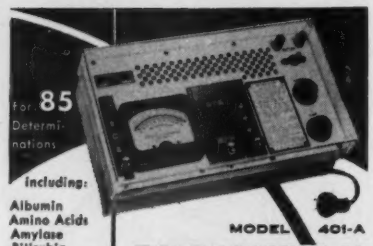
•

Then there's the story of a wife who went in front of a judge and said, "All I am asking is that my husband should leave me the way he found me."

Slightly startled, the judge said, "But, lady, that's impossible."

"Why impossible? He found me a widow, didn't he?"

—D. D.



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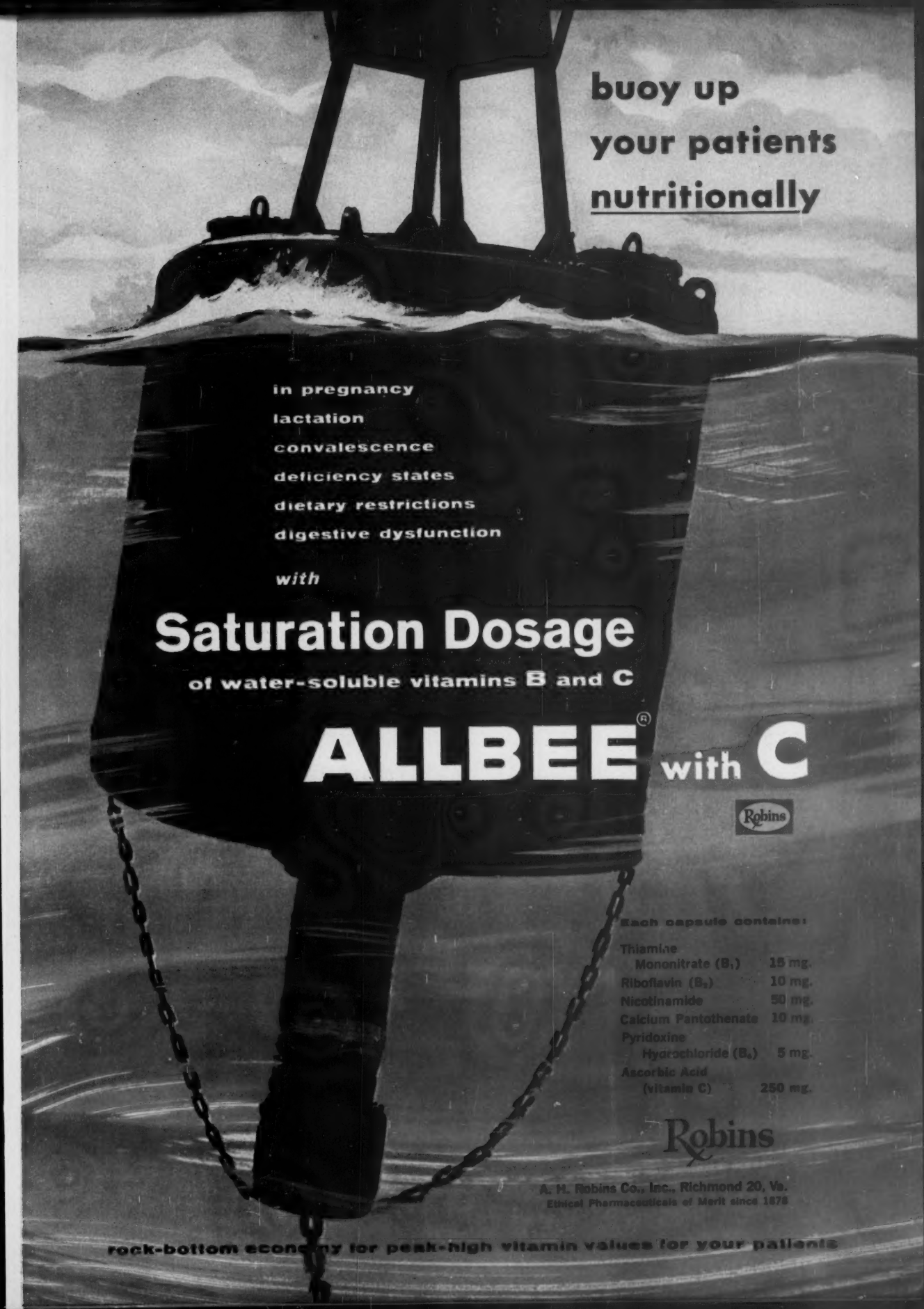
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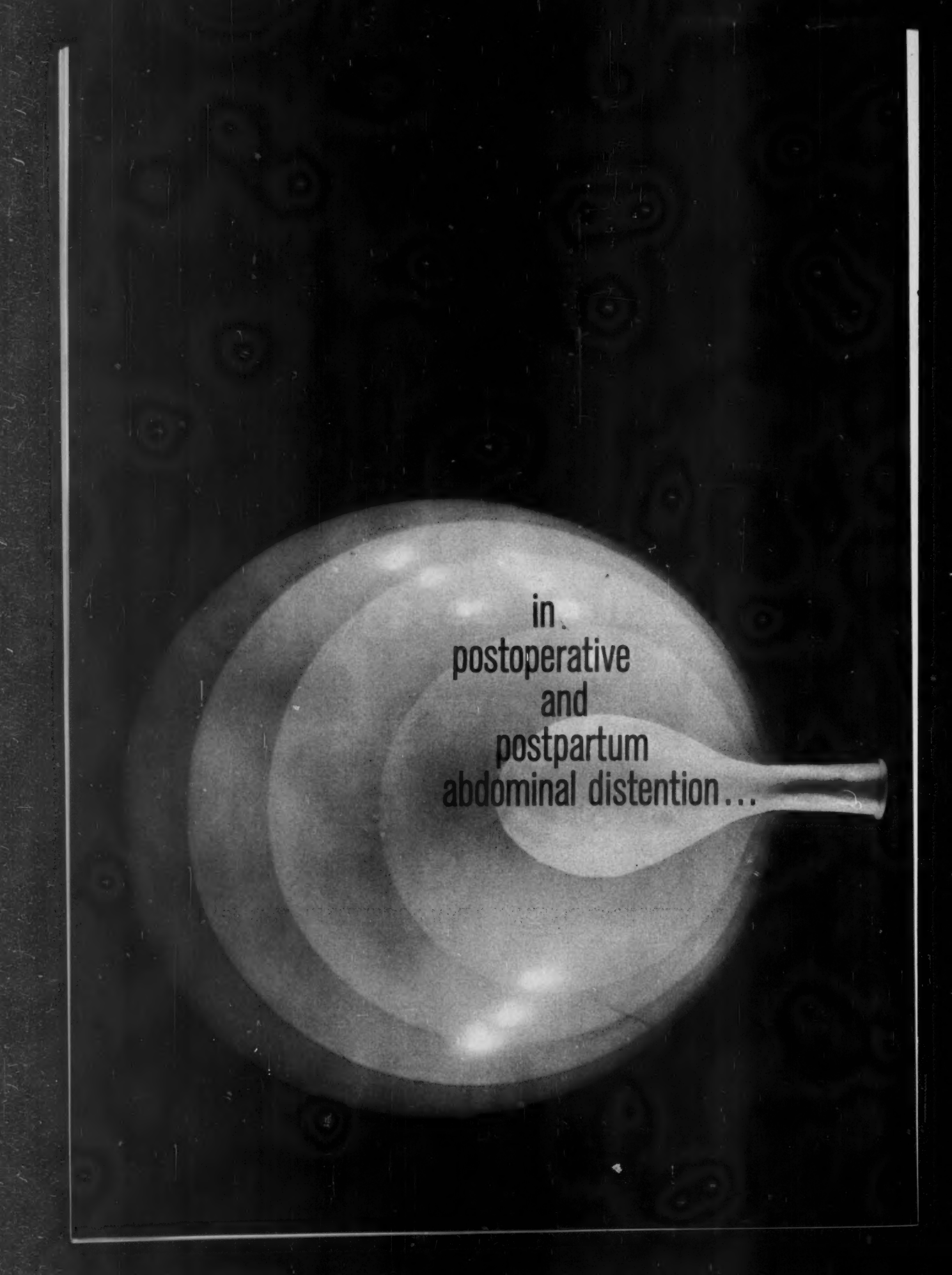
in
postoperative
and
postpartum
abdominal distention...

Because it stimulates peristalsis, URECHOLINE helps restore normal gastrointestinal function after surgery or childbirth—without subjecting the patient to the discomfort of enemas, intubation, and suction apparatus.

Therapeutically, URECHOLINE is widely used to relieve abdominal distention by facilitating expulsion of gas and promoting defecation. Prophylactically, giving URECHOLINE soon after surgery or childbirth often prevents the development of abdominal distention.

Other indications: Paralytic ileus resulting from trauma, infections, or neurogenic disorders; megacolon; prophylaxis and therapy of postoperative and postpartum urinary retention; neurogenic bladder; to counteract such side effects of ganglionic blocking drugs as paralytic ileus and urinary retention.

Administration and dosage: Usual oral dosage is 10 to 30 mg. three or four times daily. Usual subcutaneous dosage is 5 mg. three or four times daily.

Supplied: 5 mg. and 10 mg. tablets, bottles of 100. 1-cc. ampuls containing 5 mg.

uncomfortable enemas and intubation

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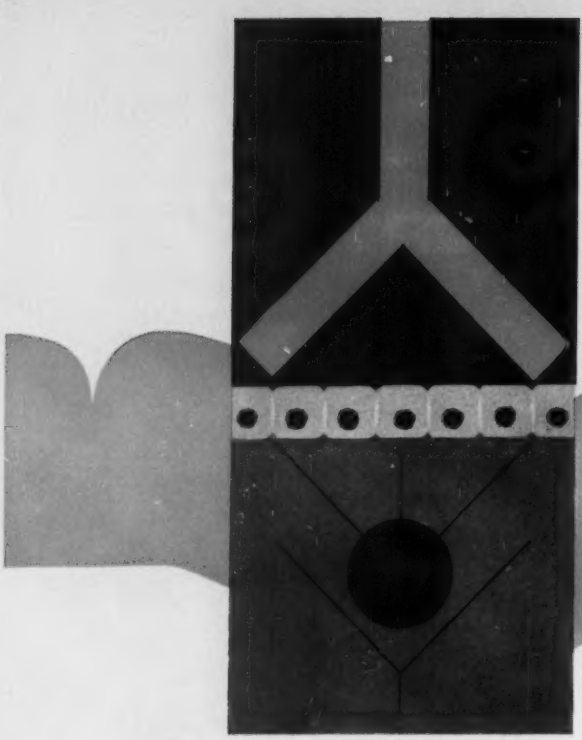

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Dulcolax®

Dulcolax — in either tablet or suppository form — insures gentle but effective bowel evacuation.

Works exclusively by contact — not by systemic absorption.

Acts on the large bowel alone.

Is equally effective whether administered orally or by suppository.

Dosage: Tablets — 1 to 3 (usually 2) at bedtime for bowel movement the following morning, or ½ hour before breakfast for a movement within six hours. Tablets are enteric coated, and must be taken whole, not chewed or crushed; they should not be taken with antacids. Suppositories — 1 at the time a bowel movement is required.

Supplied: Dulcolax® (brand of bisacodyl). Yellow enteric-coated tablets of 5 mg. in boxes of 6 and bottles of 100. Suppositories of 10 mg. in boxes of 6. Under license from C. H. Boehringer Sohn, Ingelheim.

Contact Laxative

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only one Schering Repetab will give your patient

NONSTOP RELIEF FROM NEW YORK TO ISTANBUL

When you prescribe medication in convenient REPETAB form, one REPETAB taken just before his jet flight leaves New York's Idlewild Airport will give your patient the benefits of the first full dose almost as swiftly as his plane soars up and out over the Atlantic. He'll enjoy a single, sustained high therapeutic level for up to 12 hours as his modern plane carries him smoothly over the 5,009 miles. And he can relax until he settles down to shish kebab at Pandeli's 12 hours later....That 12-hour flight to Istanbul is just over the horizon. Modern, dependable REPETABS are here now!

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FOR STAPHYLOCOCCAL INFECTIONS IN OR OUT OF THE HOSPITAL

CHLOROMYCETIN®

Recent evidence indicates that "...resistant staphylococci are no longer confined to hospitals and are increasing in the community at large."[1] CHLOROMYCETIN, however, still inhibits most strains of staphylococci,[2-5] including over 90 per cent of those commonly isolated in hospital-acquired infections.[2,6-8]

In a study[9] of pneumonia complicating Asian influenza, bacterial sensitivity to CHLOROMYCETIN was found in 94 per cent of strains of staphylococci isolated from patients who, presumably, had been admitted to hospital with staphylococcal pneumonia, and in 91 per cent of strains isolated from patients who probably had acquired staphylococcal pneumonia after admission to hospital.

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is available in various forms, including Kapseals® of 250 mg., in bottles of 16 and 100.

CHLOROMYCETIN is a potent therapeutic agent and, because certain blood dyscrasias have been associated with its administration, it should not be used indiscriminately or for minor infections. Furthermore, as with certain other drugs, adequate blood studies should be made when the patient requires prolonged or intermittent therapy.

REFERENCES: (1) Hurst, V., & Grossman, M.: *California Med.* 89:107, 1958. (2) Borchardt, K. A.: *Antibiotics & Chemother.* 8:504, 1958. (3) Holloway, W. J., & Scott, E. G.: *Delaware M. J.* 30:175, 1958. (4) Waisbren, B. A., & Strelitzer, C. L.: *Arch. Int. Med.* 101:397, 1958. (5) Markham, N. E., & Shott, H. C. W.: *New Zealand M. J.* 57:55, 1958. (6) Blair, J. E., & Carr, M.: *J.A.M.A.* 166:1192, 1958. (7) Godfrey, M. E., & Smith, I. M.: *J.A.M.A.* 166:1197, 1958. (8) Caswell, H. T., *et al.*: *Surg., Gynec. & Obst.* 106:1, 1958. (9) Oswald, N. C.; Shooter, R. A., & Curwen, M. P.: *Brit. M. J.* 2:1305 (Nov. 29) 1958.

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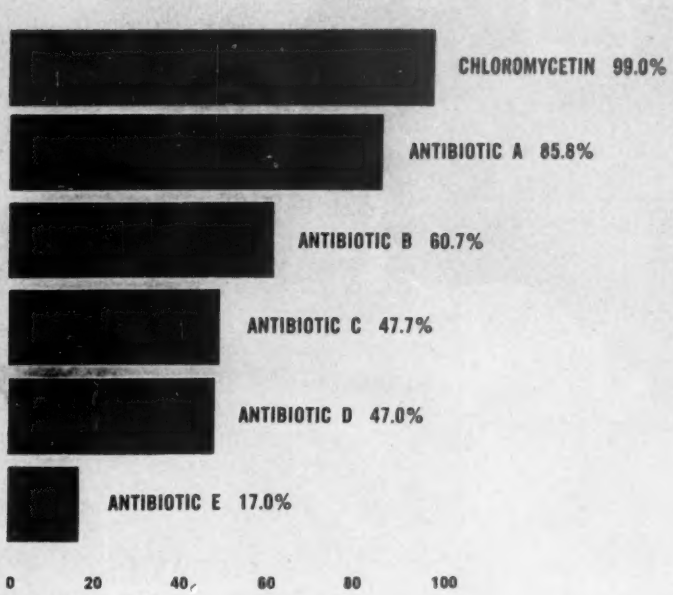
IN VITRO SENSITIVITY OF 281 CULTURES OF STAPHYLOCOCCI TO CHLOROMYCETIN AND TO FIVE OTHER ANTIBIOTICS*



*Adapted from Borchardt.[2] Staphylococci studied were isolated from clinical and pathological material from patients in the Denver area.

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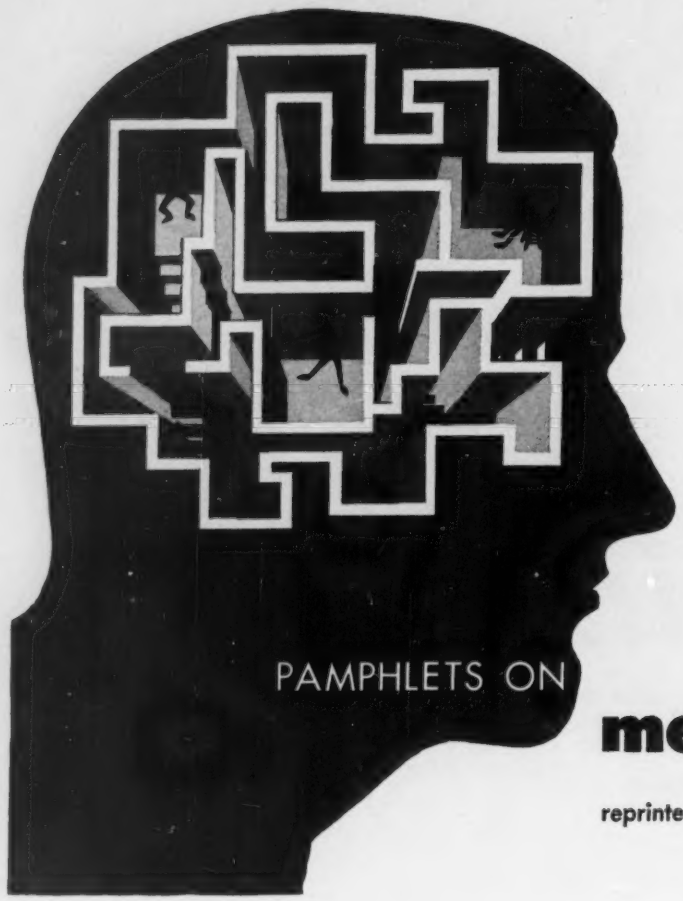

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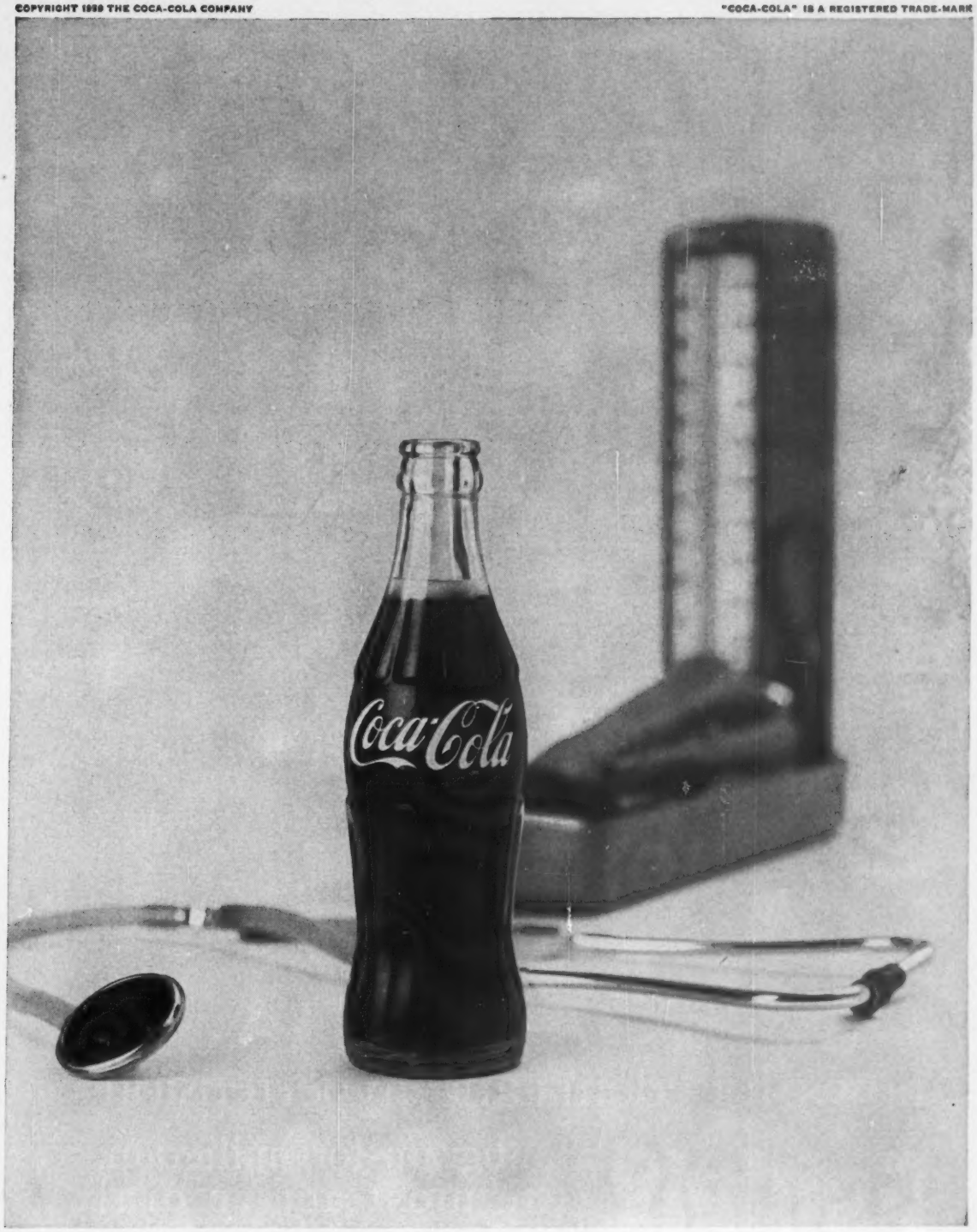

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as "the pause that refreshes" with ice-cold Coca-Cola.

now...for edema and hypertension

Esidrix
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milligram-for-milligram,
the most active oral
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New diuretic-antihypertensive with high degree of activity, low toxicity

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Patients unresponsive to chlorothiazide and mercurials in certain cases respond readily to Esidrix.

Use in hypertension: Esidrix may be used alone or in combination with other antihypertensive drugs to bring about effective lowering of blood pressure. The drug potentiates the action of all other antihypertensive agents, including SINGOSERP, SERPASIL and APRESOLINE. Dosage (and side effects) of other agents often can be reduced when they are given with Esidrix.

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Dosage: Esidrix is administered orally in an average dose of 75 to 100 mg. daily, with a range of 25 to 200 mg. A single dose may be given in the morning or tablets may be administered 2 or 3 times a day.

Supplied: TABLETS, 25 mg. (pink, scored); bottles of 100.
TABLETS, 50 mg. (yellow, scored); bottles of 100.

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- following neurosurgical diagnostic procedures
- in infections, intra-abdominal disease, and carcinomatosis
- after nitrogen mustard therapy

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ANTIEMETIC DOSAGE:
Intravenous: 8 mg. average single dose
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Oral: 10-20 mg. initially; then 10 mg. t.i.d.

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you've heard the question...

why "white" bread?

why not whole wheat?

Sometimes... you hear the question—why "white" bread? Why not whole wheat or a specialty loaf containing darker fractions of the wheat berry?

There are reasons:

First, most people eat "white" bread, buns, biscuits and other products of enriched flour for the most compelling of all reasons. They like them. They prefer the appearance, flavor and texture of enriched products to whole wheat.

Authorities consider enriched and whole wheat products to be nutritional equivalents in planning good diet. Enrichment adds niacin, riboflavin, thiamine and iron to bread and flour without adding calories or cost. Enrichment is in large measure responsible for the generous supplies of these nutrients in national diet. Made most frequently with milk or milk solids, today's breadstuffs also contribute calcium as well. As for protein, the amino acid composition of all wheat products becomes complete and adequate when eaten—as they usually are—with proteins of animal origin.

Which leaves only calories. And if you check calorie tables, you will find breadstuffs among foods relatively low in caloric values, with insignificant differences between enriched and whole wheat. Other nutrients, for which Recommended Daily Dietary Allowances are specified by the National Research Council, are found in neither enriched nor whole wheat products—but come most easily from other foods in a balanced diet. Finally, no other one popular food contributes as much at so low a cost as breadstuffs.

If you still ask, But why "white" bread?... then consider further: The absence of roughage in enriched bread enables sensitive digestive tracts to handle it without needless irritation. Since roughage tends to speed the passage of food, there may be even more nourishment actually available in diet with enriched rather than whole wheat products.

But in normal diet—eat either enriched or whole wheat, or both for variety, as you prefer.

Citations in support of the above statements would fill several pages. If you still have questions of enriched versus whole wheat, may we send you a free copy of the authoritative booklet, "Role of Wheat and Wheat Products in Human Nutrition"? This reprint of an article from "Physiological Reviews" provides a broad over-view of the subject. Please write or use the coupon.

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and whole wheat flour foods are listed among the "Essential Four" food groups set up by the Bureau of Human Nutrition—U.S. Dept. of Agriculture. Diet selected from these foods provides ample protein, vitamins and minerals.

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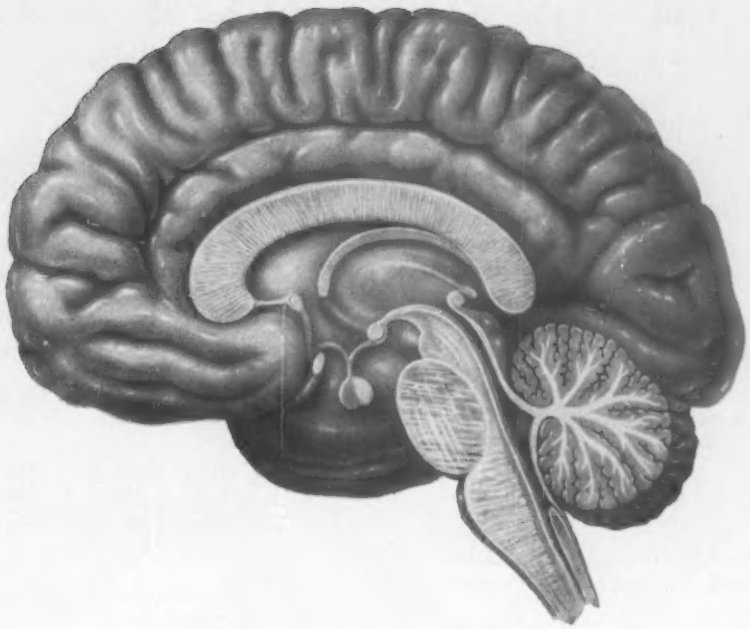
CONTROLS BOTH ANXIETY AND PSYCHOMOTOR AGITATION THROUGH DUAL ACTION

PROZINE simultaneously controls anxiety and tension as well as psychomotor agitation. This multiple effect enables the physician to exert more complete control over the emotionally disturbed patient.

PROZINE is indicated in patients with primary emotional disturbance, in patients emotionally disturbed by primary organic disease, and in patients with emotional disturbance unrelated to their organic disease.

PROZINE is useful in moderate to severe emotional disturbances manifested by apprehension and agitation or associated with insomnia, depression, nausea and vomiting, gastrointestinal disturbances, alcoholism, menopausal or premenstrual syndromes. PROZINE in the recommended dosage (1 or 2 capsules, 3 or 4 times daily) provides symptomatic control over these manifestations with the unmistakable benefits of a low-dosage regimen.

In emotionally disturbed patients, the effective dose of PROZINE is diminished to the point where the incidence and severity of side-effects and toxic reactions are minimal; the patient is calm, tranquil, and amenable to additional therapy, whether it is psychiatric, medical, or educational. *Trademark



The physician will see many applications for PROZINE in his day-to-day practice. Prominent among these is its use in overly apprehensive medical, surgical, and obstetrical patients as well as children, adolescents, and elderly patients suffering behavioral disturbances. Often, emotionally disturbed patients receiving analgesics, antihypertensives, barbiturates, anticholinergics, estrogens, or corticoids for organic disorders respond significantly better when PROZINE is added to the therapeutic regimen. Dosages of such drugs, consequently, may be dramatically reduced.

SUPPLIED: PROZINE—Bottles of 50 capsules. Each green and white capsule contains 200 mg. meprobamate and 25 mg. promazine hydrochloride.

Comprehensive literature is available

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THE BRIGHT SIDE

by E. K. H.

The town's leading citizen was finishing a speech to the local chamber of commerce on money and the fact that we Americans concentrate so much on acquiring it.

"Remember, gentlemen," he intoned pontifically, "it isn't *money* that will heal a broken heart or mend the fragments of a broken dream! Money can't bring joy to a divided home or make up for the defects of a dissipated life!"

He paused solemnly for a moment, then continued. "I'm referring, of course, to *Confederate money.*"

•

We like the title of Jerri Sothern's album of Deep South drinking songs—"Southern Fried."

•

An opera lover, walking along the street one early spring day, was passing a pet shop, when, from within, came the most beautiful voice he had ever heard. He dashed into the shop where a canary fully as lovely as its voice was trilling "The Bell Song" from "Lakme."

"That bird!" he cried. "Is it for sale? I must have it!"

"Yes, isn't it wonderful?" answered the proprietor. "It can be had for $500."

"Five hundred dollars!" cried the man. "Why that's ridiculous."

But as the bird continued its melodious warbling, he knew he was licked.

"O. K. I'll take it right home with me."

"Fine," said the proprietor. He reached into the next cage and picked up a scrawny, featherless crow and deposited it next to the songbird.

"Wait a minute," cried the man. "What are you doing?"

"I forgot to tell you—this bird goes along with yours."

"*That* mangy thing! What's the big idea?"

"Well, you see," was the explanation, "he's the *arranger!*"

•

Russell Crouse, co-author of "Life with Father," "State of the Union," etc., was asked by a music lover if he liked operettas.

"Well, yes," quipped Crouse, "if they are telephone operettas."

The bookkeeper excitedly informed the owner of a comparatively new business that the firm was out of the red for the first time.

"Wonderful!" exclaimed the proud businessman. "Make up two dozen copies of that statement immediately and mail them to the bank and all my creditors."

"Sorry," said the bookkeeper. "We haven't any black typewriter ribbon; we never needed it before."

"Well," ordered the boss, "go out and buy some."

"Can't," came the determined answer. "That would put us right back in the red again."

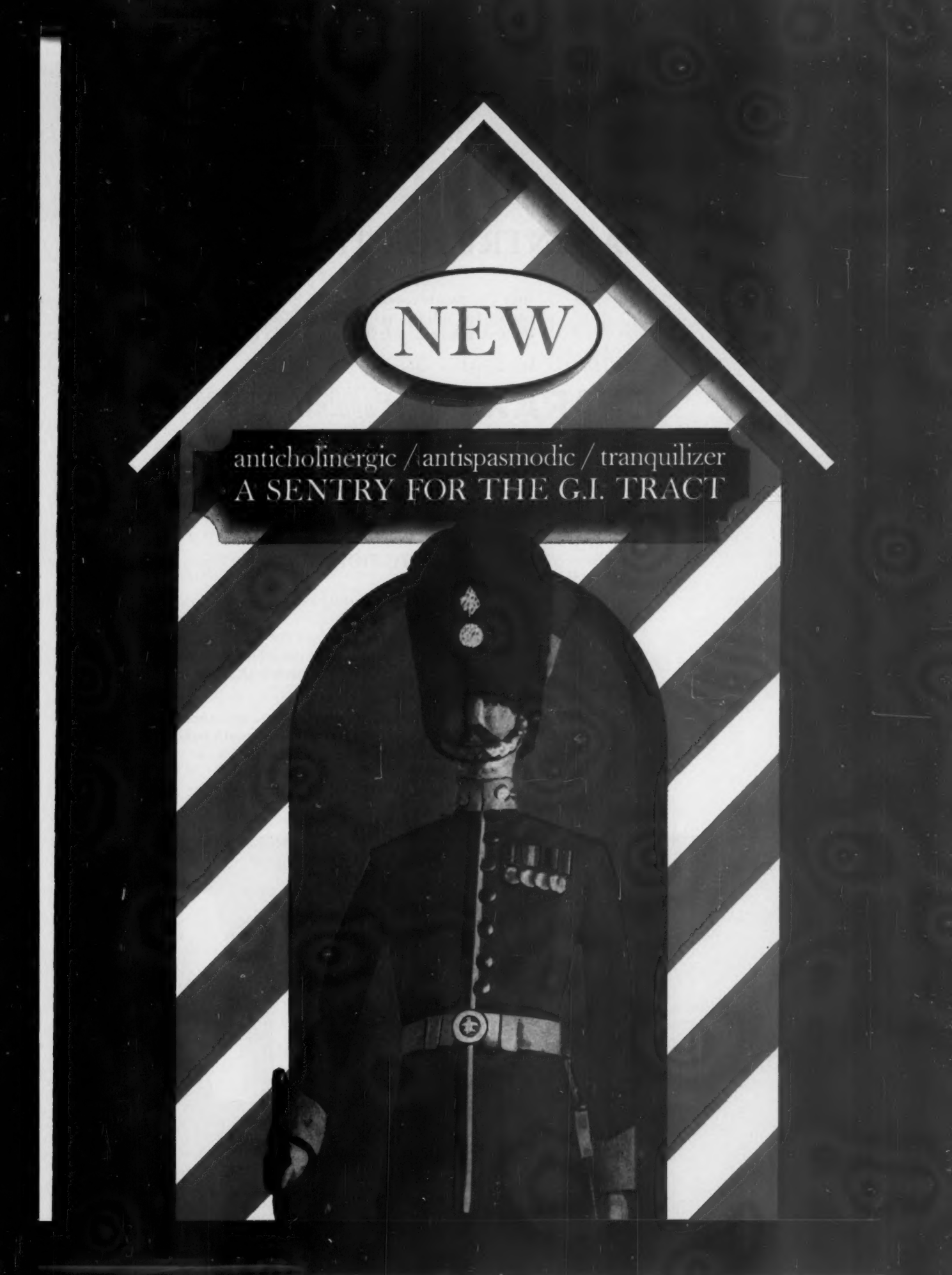
•

According to Louis Sobol, George Jessel, who will speak on any subject, anywhere, any time, had just been hurriedly engaged to deliver the eulogy at a recent funeral service.

After bringing tears to his own and everyone else's eyes, Jessel suddenly glanced down into the coffin.

"Holy smoke," he cried. "I *knew* this man!"

"Everyone of them was a football star in college, and even now they want to be sure they're recognized."


NEW
anticholinergic / antispasmodic / tranquilizer
A SENTRY FOR THE G.I. TRACT

NEW: A SENTRY FOR THE G.I. TRACT

Since G.I. disorders present multiple difficulties, perhaps you will welcome *one* medication that combats the most prominent and most troublesome symptoms.

ENARAX *protects against*

hypersecretion
hypermotility
hyperirritability
hyperemotivity

ENARAX combines a new long-acting anticholinergic (antisecretory-antispasmodic[1]) with the proven antisecretory-tranquilizer[2-6] (ATARAX®) to relieve pain, spasm, hyperacidity and disease-induced tension. With this unique anticholinergic, just two tablets daily proved clinically effective in 428 out of 490 patients with a wide variety of gastrointestinal disorders.[1,2,7]

Selective postganglionic action on the G.I. tract minimizes side effects. Of 512 patients treated to date, reactions were usually mild, transient and easily reversed. Mouth dryness, blurring of vision, dizziness, urinary hesitancy either disappeared with continued use or were controlled by reducing the dosage.

ENA

ENARAX one tablet at breakfast
one tablet at bedtime

full-time relief in

peptic ulcer	gastritis	duodenitis
functional bowel syndrome	gastroenteritis	hiatus hernia (symptomatic)
ulcerative colitis	pylorospasm	genitourinary spasm
biliary tract dysfunctions	cardiospasm	dysmenorrhea

Each ENARAX tablet contains:
Oxyphencyclimine HCl . . . 10 mg.,
Hydroxyzine HCl (ATARAX®) . . . 25 mg.

Dosage: One-half to one tablet twice daily – preferably in the morning and before retiring. The maintenance dose should be adjusted according to therapeutic response. Use with caution in patients with prostatic hypertrophy or glaucoma.

Supplied: In bottles of 60 black-and-white scored tablets.

References: 1. McHardy, G., et al.: Paper presented at Postgraduate Course in Gastroenterology, University of California School of Medicine, San Francisco, California, January 27, 1958. 2. Strub, I. H., and Carballo, A.: To be published. 3. Schuller, E.: Gaz. des Hôpitaux *10*:391 (Apr. 10) 1957. 4. Farah, L.: Internat. Rec. Med. *169*:579 (June) 1956. 5. La Barre, J.: Compt. rend. Soc. Biol. (Paris) *150*:1807 (Oct.) 1956. 6. Harrisson, J. W. E., et al.: Paper presented at the 4th Pan-American Congress of Pharmacy and Biochemistry, Washington, D. C., November 3-9, 1957. 7. Data in Roerig Medical Department files.

ROERIG Rx

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Science for the World's Well-Being

Victim of Overeating and "Oversitting"

℞

BIPHETAMINE®

A 'STRASIONIC' RELEASE ANORETIC RESIN

- **10-14 Hour Appetite Curb**
- **10-14 Hour Mild Invigoration**
- **Predictable Weight Loss...**
  a comfortable 1 to 3 lbs. a week in 9 out of 10 cases

In many instances both appetite limitation and mild invigoration ('Biphetamine') are required to effect the balance between caloric intake and energy output necessary for predictable weight reduction and control. Since 'Strasionic' release is employed, the desired therapeutic action is uniform, predictable and comfortable.

Biphetamine may be prescribed for the obese hypertensive, arthritic, diabetic, pregnant, menopausal, aged, or pre-operative patient. Use with care in patients hypersensitive to sympathomimetic compounds, in cases of coronary disease or severe hypertension.

- **Single Capsule Daily Dose 10 to 14 hours before retiring**

3 STRENGTHS

List No. 675
BIPHETAMINE® '20' Resin
Each black capsule contains:
d-amphetamine ..... 10 mg.
dl-amphetamine ..... 10 mg.
as resin complexes

List No. 676
BIPHETAMINE® '12½' Resin
Each black and white capsule contains:
d-amphetamine .....6.25 mg.
dl-amphetamine .....6.25 mg.
as resin complexes

List No. 895
BIPHETAMINE® '7½' Resin
Each white capsule contains:
d-amphetamine .....3.75 mg.
dl-amphetamine .....3.75 mg.
as resin complexes

℞ Only. Caution: Federal law prohibits dispensing without prescription.

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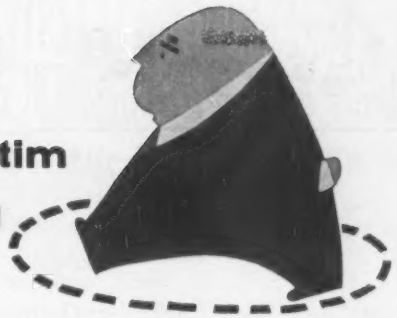
ROCHESTER, N.Y., U.S.A.
Originators of 'Strasionic' (sustained ionic) Release



Victim of Overeating

℞ NEW

Appetite Limitation Only

IONAMIN™

A 'STRASIONIC' ANORETIC

PHENYL-*TERT.*-BUTYLAMINE RESIN

- **10-14 Hour Appetite Curb**
- **Predictable Weight Loss...**
  a comfortable .221 lbs. per day in average case

BALANCE

In many instances, appetite limitation only ('Ionamin') is required to effect the balance between caloric intake and energy output necessary for predictable weight reduction and control. Since 'Strasionic' release is employed, the desired therapeutic action is uniform, predictable and comfortable.

Ionamin may be prescribed for the obese arthritic, diabetic, pregnant, menopausal, aged, or pre-operative patient, and may be used with caution in hypertensive or cardiovascular disease.

- **Single Capsule Daily Dose 10 to 14 hours before retiring**

2 STRENGTHS

List No. 904

IONAMIN™ '30'

Each yellow capsule contains: phenyl-tert.-butylamine .. 30 mg. as a resin complex

List No. 903

IONAMIN™ '15'

Each grey and yellow capsule contains: phenyl-tert.-butylamine .. 15 mg. as a resin complex

℞ Only.
Caution: Federal law prohibits dispensing without prescription.

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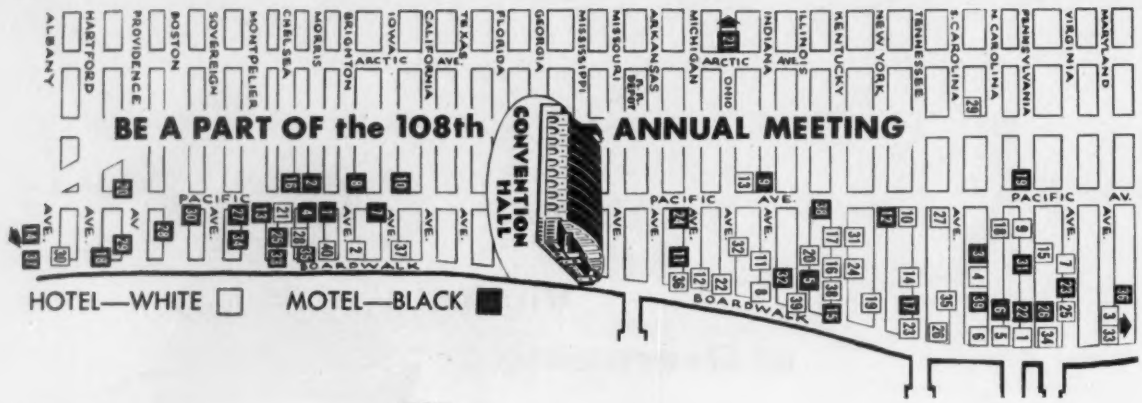
Originators of 'Strasionic' (sustained ionic) Release



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16 Central Pier
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Be sure to give six choices of hotels or motels

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Please reserve the following Hotel or Motel accommodations:

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.....Suite (parlor and bedroom) for.....person(s). Rate $.....

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Rooms will be occupied by: *(Please attach list of additional names if you do not have sufficient space here. Also list ages of children, if any.)*

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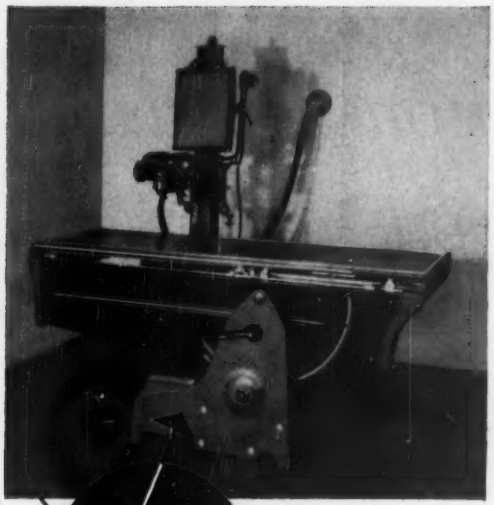
If you are a technical exhibitor, be sure to give name of firm and individuals to occupy room or rooms reserved.



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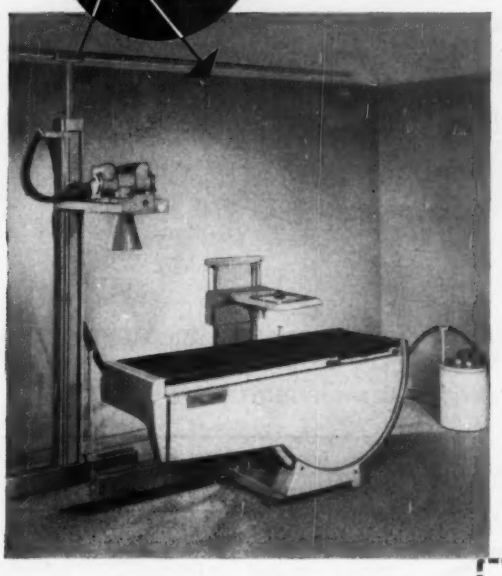

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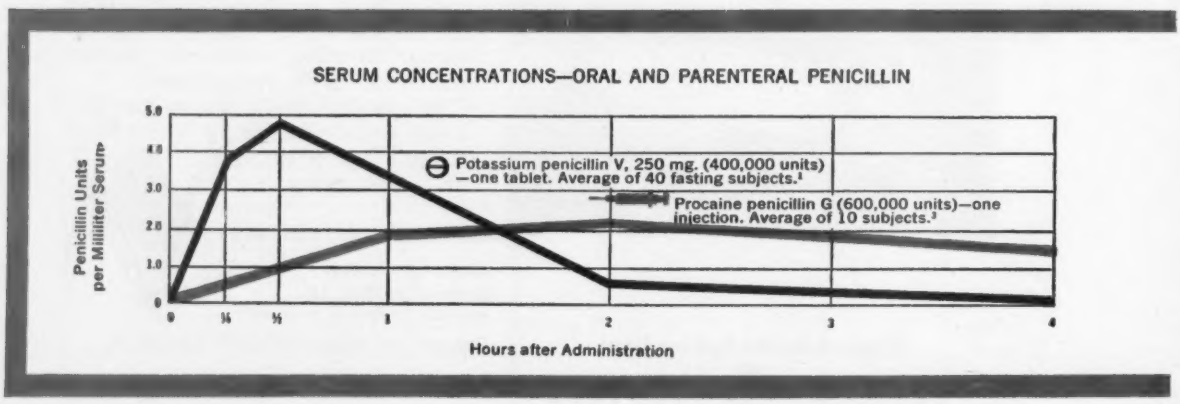
the speed of action you want the reliability you need

In recent studies involving 107 subjects, effective penicillin blood levels were *consistently* produced within 15 minutes after administration of oral potassium penicillin V. Peak levels were obtained within a half-hour. Even after two hours, effective penicillin blood levels still persisted in *every* subject. At four hours, demonstrable blood levels existed in 93 per cent of subjects.[1-2]

PEN·VEE K may be prescribed for
all infections responsive to oral penicillin
. . . and even many usually treated with parenteral penicillin



1. Peck, F.B., Jr., and Griffith, R.S.: Antibiotics Annual 1957-1958, Medical Encyclopedia, Inc., p. 1004. 2. Wright, W.W., and Welch, H.: Antibiotic Med. *5*:139 (Feb.) 1958. 3. White, A.C., et al.: Antibiotics Annual 1955-1956, Medical Encyclopedia, Inc., p. 490.

The antibiotic that is prescribed most often for common bacterial infections . . .

penicillin

In a form that produces high penicillin blood levels rapidly and reliably . . .

potassium penicillin V

In two dosage strengths and preparations to assure acceptance by patients . . .

PEN·VEE® K

Liquid: Penicillin V Potassium for Oral Solution; Tablets: Penicillin V Potassium, Wyeth

LIQUID

flexibility of dosage form and high potency assure acceptability of full therapeutic dosage

SUPPLIED: *Liquid*: raspberry-flavored, 125 mg. (200,000 units) per 5-cc. teaspoonful; peach-flavored, 250 mg. (400,000 units) per 5-cc. teaspoonful. Supplied as vials of powder to make 40 cc. *Tablets*: 125 mg. (200,000 units) and 250 mg. (400,000 units) in vials of 36.

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Leukemia.....

'LEUKERAN'® brand

CHLORAMBUCIL (formerly known as C. B. 1348)

FOR CHRONIC LYMPHOCYTIC LEUKEMIA

A derivative of nitrogen mustard, it has provided amelioration of follicular lymphoma, lymphocytic lymphoma with or without leukemia, and Hodgkin's disease.

Sugar-coated Tablets of 2 mg.

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FOR CHRONIC MYELOCYTIC LEUKEMIA

'Myleran' has been reported to induce remissions, lasting up to two years, in chronic myelocytic leukemia. In addition to the decrease in total white cell count and a selective reduction of immature myeloid cells, it usually gives, early after its administration, a rise in hemoglobin level and pronounced subjective improvement.

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FOR ACUTE LEUKEMIA AND CHRONIC MYELOCYTIC LEUKEMIA

'Purinethol' provides worth-while temporary remissions, either partial or complete, in a high percentage of patients. In general, a higher proportion of children than adults with acute leukemia respond favorably.

Tablets of 50 mg.

Facilities for complete and frequent blood counts must be available for patients receiving 'Leukeran', 'Myleran' or 'Purinethol'.

Full information about these products will be sent on request.

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(Continued from page 212)

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ENT: Grp est since '47; NW; modern comp clin bldg; 2 hosp avail; to $20,000 start

EYE: 5-man grp Virginia near Wash., D. C., office share agreement or any agreement applicant may wish, financial assistance offered initially if required

G.P.: (a) no surg; 3-man assn; Calif nr San Fran; $1200 1st mo, then up; prtnrshp 1-yr; (b) w/surg & ob; steady income $18,000; 4-man grp; NEng manuf twn (c) w/minor surg, some indus; 6 man grp; So; $1000 a mo. & 50% of extras

INDUS. MED. & SURG.: F/T assn, 2 men; $10,000; MW

INSURANCE: desk job; NEng; orthop trng nec; $8,000, increments

INTERNIST: Cardiology or GE if interested, $15,000 start, future prtnrshp, clinic of 14 young doctors, hunting & fishing country of Minn

MEDICAL DIRECTOR: Railroad, Internist preferred, applicants should come from transportation industry, new medical dept. being established, N.Eng., to $15,000

NEUROSURGEON: assn w/2 highly qual men; MW; income open

OB-GYN: (a) 2nd in dept; Calif grp est 5 yrs; to $1000; (b) asst or assoc; Ill; 25-yr pract w/Cert man; compensation, working conditions 'no trouble'; hosp & Univ med schl connections

ORTHOP. SURG.: 2nd in dept now, head Dept in short while; MW clinic of yng men, est 11 yrs; to $16,000 w/special consideration

PEDIATRICIANS: familiar w/all kinds of jobs, all sections of country, paying the right salary

RADIOLOGIST: (a) assoc; lge active pract; Minn; referrals from 75 doctors; at least $15,000 1st yr, can be increased; (b) for 92 bed genl hosp; also direct cancer clin & Consultant VA mental hosp; West; man leaving netted $29,000 in '58

STUDENT HEALTH: (a) F/T staff; Jul 1st; MW; to $10,000 (b) GP or internist; opptny teh & further study; to $10,000; So

SURGEON: hosp, So, to $15,000 1st yr

TBC: Med. Dir. & Supt; Calif; FCCP or Elig; to $12,000 & mtn for doctor & family

Upon request one of our applications will be mailed to you. Write us today—a post card will do.

MEDICAL HEALTH OFFICER—FOR ESTABLISHED urban and rural county health department in northwestern Ohio; population, 140,000; salary $12,000, good personnel policies, vacation, retirement, and sick leave. Address inquiries to: W. T. Gravius, 5525 W. Bancroft Street, Toledo, Ohio. C

WANTED — BOARD CERTIFIED PHYSIATRISTS—For full time hospital practice at Beckley Memorial Hospital, Beckley, West Virginia; starting compensation $20,000; progressive pay scale. For details address: The Clinical Director, Miners Memorial Hospital Association, 1427 Eye Street, N. W., Washington 5, D. C. C

ORTHOPAEDIC SURGEON — YOUNGER CERTIFIED established orthopaedic surgeon, Chicago, desires qualified or Certified associate; excellent hospital facilities and expanding practice; adequate vacation and meeting time; minimal emergency work; $12,000-$15,000 plus bonus potential to start. Box 8027 C, % AMA.

WANTED—BOARD CERTIFIED PSYCHIATRIST: FOR full time hospital practice in professional care program of the Miners Memorial Hospitals; starting compensation $20,000; progressive pay scale. For details address: The Clinical Director, Miners Memorial Hospital Association, 1427 Eye Street, N. W., Washington 5, D. C. C

OBSTETRICIAN-GYNECOLOGIST WANTED — EXcellent opportunity, progressive medical group, community 10,000; area 40,000; new air-conditioned, fully equipped building; partnership after first year; good hospital facilities; 40 or under; Board qualified. Box 8049 C, % AMA.

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UROLOGIST—BOARD OR ELIGIBLE FOR CHIEF, OF Section in active 450 bed GM&S hospital, salary to $16,000 depending on qualifications; citizenship required; liberal vacation and retirement benefits; desirable community. Contact: Manager, Veterans Administration Center, Shreveport, Louisiana. C

GENERAL PRACTITIONER—DESIRING EARLY AND permanent group practice association; capable of good obstetrics and internal medicine; starting salary later; partnership. The Palm Springs Medical Clinic, 1091 N. Palm Canyon, Palm Springs, California, Fairview 4-1531. C

WANTED—A SUCCESSOR FOR MY WELL ESTABlished and lucrative office practice in city of 150,000 in central Pennsylvania; practice easily transferrable; retiring on account of ill health; will be happy to furnish additional information if you really mean business. Box 7909 C, % AMA.

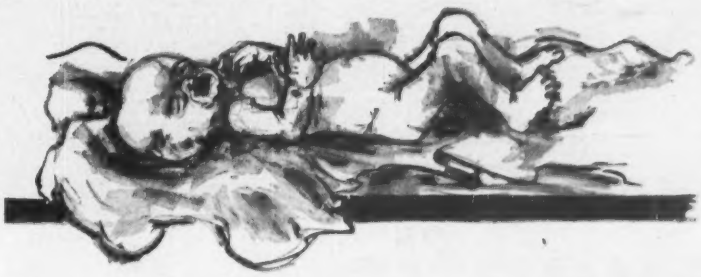
INDUSTRIAL PHYSICIAN TO DIRECT INDUSTRIAL medicine program with opportunity to perform some toxicological research in a new field within the chemical industry; must be U. S. citizen; New York state location. Send complete resume, and salary requirements to: Box 7540 C, % AMA.

GENERAL PRACTITIONER—DESIRING EARLY AND permanent group practice association; capable of good obstetrics and internal medicine; starting salary later; partnership. The Palm Springs Medical Clinic, 1091 N. Palm Canyon, Palm Springs, California, Fairview 4-1531. C

ELEVEN MAN MID IOWA GROUP NEEDS SECOND pediatrician; Board qualified; early partnership. Write: Box 8057 C, % AMA.

VERSATILE FURACIN

effective by intrapleural instillation[1]



the situation: Four-month-old infant with staphylococcal pneumonia and empyema resistant to most antibiotics was allergic to antibiotic chosen after sensitivity tests. Thoracentesis produced 30-40 cc. of creamy, purulent fluid. Organism was Staphylococcus aureus, coagulase positive.

then Furacin was instilled: 0.2% Solution was diluted equally with physiologic saline and 10 cc. of mixture instilled twice daily into pleural space, with suction catheter clamped off for 1 hour. Fluid almost immediately became thinner and less viscous. Twenty-four hours later infant was less irritable, voluntarily started taking food. Instillations stopped. FURADANTIN® Oral Suspension prescribed. Recovery uneventful.

1. Perkins, J. L.: Kansas State M. J. (to be published).

FURACIN®

brand of nitrofurazone

FURACIN has been in clinical use for more than 13 years. Today it is one of the most widely prescribed single topical antibacterial agents. Like other nitrofurans, FURACIN remains effective, even in pus, sera or exudates, against pathogens which have developed—or are prone to develop—resistance to antibiotics.

NITROFURANS—a unique class of antimicrobials—neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK

GENERAL PRACTITIONER—TO JOIN ESTABLISHED group in private practice, college town, drawing population 20,000; offices available; hospital same building; no initial investment; above average income. Write: Dr. R. Lee Cooper, Warrensburg Medical Center, Warrensburg, Missouri. C

PEDIATRICIAN — YOUNG MALE; UNIVERSITY trained; certified or Board eligible; established 7 man specialty group with university affiliation needs third pediatrician; salary plus percentage; early partnership. The Buckhead Clinic, 3451 Peachtree Road, N.E., Atlanta 5, Georgia. C

WANTED — INTERNISTS: BOARD CERTIFIED OR Board eligible if well qualified; also vacancy in pulmonary tuberculosis; must be United States citizens; foreign graduates eligible if on approved list. Write: Manager, Veterans Administration Consolidated Center, Wadsworth (Leavenworth), Kansas. C

PSYCHIATRIST WANTED—MINIMUM 3 YEARS APproved residency; to associate with Board psychiatrist in central Pennsylvania; practice includes private psychiatric hospital and out-patients; attractive salary guaranteed. Box 8073 C, % AMA.

WANTED—AMERICAN BOARD SPECIALISTS; PHYsicians interested in group or private practice; teaching research, public health or industrial medicine; National and international services. Our 62nd Year. Woodward Medical Bureau, 185 N. Wabash Avenue, Chicago. C

CITY OF SPRINGFIELD, MASSACHUSETTS, SEEKS services of Chief of Professional Services and 4 staff physicians for new chronic disease hospital; salary open. Address applications to: Personnel Director, City Hall, state training, experience and salary desired. C

WANTED — YOUNG GENERAL PRACTITIONER OR internist; association with two physicians; partnership; well established clinic, southern West Virginia; open staff hospital same city; salary $12,000; percentage or partnership later. Box 8032 C, % AMA.

PHYSICIAN WANTED—ACTIVE MEDICAL SERVICE; average salary $8,330 to $11,355 but higher with additional qualifications; liberal fringe benefits; resort city on Lake Erie. Write: Manager, Veterans Administration Hospital, Erie, Pennsylvania. C

ORTHOPEDIST OR GENERAL SURGEON — BOARD Certification not required; active GM&S hospital; salary range $9,860 to $16,000, depending on qualifications; excellent fringe benefits. Apply: Manager, Veterans Administration Hospital, Poplar Bluff, Missouri. C

OPENING ON STAFF FOR MALE PHYSICIAN INtending career in occupational medicine; graduate approved school, not over 45; progressive chemical company, Baton Rouge, Louisiana; submit detailed qualifications in first letter. Box 8066 C, % AMA.

(Continued on next page)

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OPPORTUNITY—DOCTOR NEEDED; COUNTY SEAT city; no doctor in county of 5,000; new clinic; hospital 20 miles; excellent potential; accredited school; pharmacist; sportsman's paradise. Contact: Alvin Berg, McClusky, North Dakota. C

WANTED—PEDIATRICIAN; BOARD ELIGIBLE OR Certified; to join two other pediatricians in southeastern city; eventual full partnership; new office building; affiliation with community hospital. Box 8051 C, % AMA.

OTOLARYNGOLOGIST—CERTIFIED OR BOARD ELIGible for association with group of Certified members; starting salary, open. Forward curriculum vitae to: Dr. E. W. Erickson, The Lynn Clinic, Detroit 17, Michigan. C

WASHINGTON STATE — GENERALIST QUALIFIED surgery wanted by small group; suburb of Seattle; generalist for small group on Puget Sound. Pacific Coast Medical Bureau, Agency, 1404 Central Tower Building, 703 Market Street, San Francisco 3. C

ASSISTANT CHIEF — RADIOLOGY SERVICE FOR Veterans Hospital, Atlanta, Georgia; a Deans Committee hospital affiliated with Emory Medical School; salary up to $16,000. Contact: Director Professional Services. C

WANTED—TWO HOUSE PHYSICIANS 75 BED GENeral hospital on the eastern seashore; nice climate; good fishing and hunting year round; good salary; apply immediately. Box 8040 C, % AMA.

FLORIDA — PHYSICIAN UNDER 35 WANTED TO associate with young general practitioner in Gulf coastal county of 8,000; Florida license required; new Hill-Burton Hospital; terms open. Box 8039 C, % AMA.

WANTED—YOUNG GENERAL PRACTITIONER TO care for my practice for two to three weeks beginning June 7; $250 per week plus quarters. Box 7570 C, % AMA.

ANESTHESIOLOGIST—BOARD ELIGIBLE OR CERTIfied; to join anesthesia staff; northern California hospital; 300 beds+. on individual fee for service basis. Write: Box 8046 C, % AMA.

ANESTHESIOLOGIST—MD FOR 50 BED GENERAL hospital in suburban Philadelphia; remuneration open; based on qualifications. Apply: Administrator, Haverford Hospital, Havertown, Pennsylvania. C

PHYSICIANS—MALE AND FEMALE; WANTED FOR children's camps; July-August; 250 member camps; free placement. Association Private Camps, 55 West 42 Street, New York 36, New York. C

PRECEPTORSHIP IN GENERAL AND VASCULAR surgery with all Board group in midwestern city; future partnership considered. Box 8058 C, % AMA.

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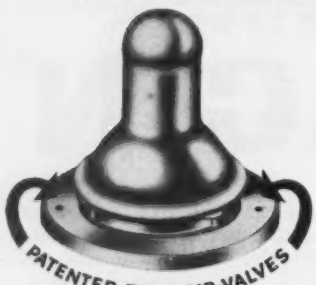

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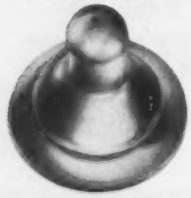
Designed to accommodate most babies. Patented Twin Air-Valves — featured in every Evenflo nipple—assure smooth formula flow, help prevent excess air swallowing and nipple collapse. Sure-seal rim seats nipple properly in cap. Pure natural gum rubber washes easily, assures sterile feeding — no ridges or grooves to retain bacteria. ONLY 10¢ each.



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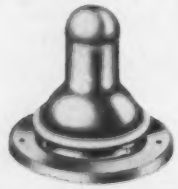

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A major Southern California (not Los Angeles) missile engineering and manufacturing organization with modern, progressive medical facilities, requires a staff physician. This man should be physically and mentally active, and desirous of making industrial medicine his career. A California license is necessary, but industrial experience is not required.

Salary is in the range of $13,000 per year, and we offer liberal fringe benefits. Please send detailed resume of training, experience and general background to Box 8047 C, c/o A. M. A.

GENERAL SURGEON WITH ORTHOPEDIC INTERest; central Nebraska 201 bed general hospital. Write: Manager, Veterans Administration Hospital, Grand Island, Nebraska. C

AVAILABLE FOR PHYSICIAN AND SURGEON; AN active practice; large completely equipped office; centrally located, and near four major hospitals; no capital needed. Reply: P. O. Box 404, Akron 9, Ohio. C

WANTED — ENT MAN; ESTABLISHED GROUP IN Indiana; Board qualified or eligible; salary open; excellent future practicing with well trained men. Box 8071 C, % AMA.

WANTED — PEDIATRICIAN TO HEAD PEDIATRIC section in a clinic in the south; must be Board Certified; early full partnership to right man. Box 8052 C, % AMA.

WANTED—RECENT GRADUATE OR YOUNG PRACticing physician to join well known ear, nose, and throat specialist; no previous training necessary; salary very high from start. Write: Box 8055 C, % AMA.

WANTED—A YOUNG MAN, BOARD ELIGIBLE OR Board Certified; for the department of obstetrics and gynecology at the Jackson Clinic, Madison, Wisconsin. Arnold S. Jackson, MD. C

GENERALIST WANTED TO AUGMENT PRESENT DEpartment of family practice in 11 man mid-Iowa group; early partnership. Write: Box 8054 C, % AMA.

THE VETERANS ADMINISTRATION HOSPITAL, Downey, Illinois and the Veterans Administration Research Hospital, Chicago, in collaboration with Northwestern University, announces a reorganized, integrated post-graduate training program in psychiatry approved for Board Certification; the facilities of eight participating hospitals and the departments, laboratories and clinics of the medical school will be fully utilized for comprehensive courses in the neurologic sciences, basic and clinical psychiatry and psychoanalysis; progressive institutional and out-patient experience with supervision in the diagnosis and therapy of all forms of behavior disorders in children, adolescents and adults makes the three years especially rewarding; other advantages offered are a physically attractive locale, a scientifically stimulating university environment, encouragement in personal psychoanalytic training, subspecialization and individual research, and rich opportunities for professional and academic advancement; salary range $3,250 to $9,890. For application forms or further information, apply to: Dr. Benjamin Boshes, Chairman, Department of Neurology and Psychiatry, The Medical School, Northwestern University, 303 East Chicago Avenue, Chicago 11, Illinois. C

PSYCHIATRIST ARKANSAS STATE HOSPITAL — Must have at least three years of approved training; preferably board certified; dynamic program of treatment; training; research and unique rehabilitation project; active association with new university of Arkansas medical center on campus of state hospital; right in city; stimulating and challenging situation with great potentialities; fine city; excellent climate; unsurpassed recreational advantages; competitive salary and fringe benefits such as social security; state retirement and liberal sick and annual leave policy; must be graduate of American or Canadian school qualify for medical licensure; Write: Granville L. Jones, MD, Superintendent, Arkansas State Hospital, Little Rock, Arkansas. C

PHYSICIANS WANTED—FOR CHICAGO AND SURrounding suburbs plus opportunities in all parts of the United States; many full and part time positions available in all specialties in industry; institutions; private associations and groups; Miss E. Ronni, our director of National placement; will be pleased to assist you in securing the position you want in the area you desire; for Chicago area call or write Mrs. N. Garland, Director, Garland Medical Placement 25 East Washington Street, Chicago 2, Illinois. ANdover 3-0145. All Inquiries are confidential. C

MEDICAL EDITOR—POSITION OF ASSOCIATE EDitor, U. S. Armed Forces Medical Journal in Washington, D. C., applicants must be graduates of approved medical schools with minimum of 4 years' experience medical editorial work; preferably on staff of medical journal or related professional periodical; competitive appointment under Federal civil service; starting salary $12,770. Forward curriculum vitae to: Bureau of Medicine and Surgery, Code 4531, Navy Department, Washington 25, D. C.

WANTED — OBSTETRICIAN-GYNECOLOGIST: SALary $15,000 per year plus apartment depending on qualifications. Box 7860 C, % AMA.

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For company operated medical facilities in Saudi Arabia

Preferably Board-certified or Board-eligible in preventive medicine (occupational medicine). To develop industrial medical service as part of company's general medical program. Liberal benefit program; modern family housing; plus educational and recreational facilities available. Write outlining personal and professional history.

Recruiting Supervisor, Box 401

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PATHOLOGIST—BOARD CERTIFIED OR BOARD ELIGIBLE for position of Chief, Laboratory Service; new, completely equipped 250 bed general hospital in west Texas; pleasant climate all year round; excellent retirement plan, life insurance, annual leave, sick leave and other benefits; salary from $11,373 to $14,685, depending on qualifications, with regular increases to $16,000. Apply: Personnel Officer, Veterans Administration Hospital, Big Springs, Texas. C

PHYSICIANS — ADMINISTRATIVE POSITIONS; INternational chemical and pharmaceutical manufacturer has unusual opportunities for physicians who are interested in combining medical background with administrative responsibilities; openings would utilize medical training and experience on a broad scientific level with advancement directed toward business management positions. Write full details including salary desired to: Box 7917 C, % AMA.

PHYSICIANS WANTED — QUALIFIED PHYSICIANS needed to work with psychiatric patients in 2,400 bed hospital+ near Chicago; salary range $6,505 to $13,970, depending upon qualifications, plus 15% additional if Board Certified, not to exceed $16,000; approved three year psychiatric residency in collaboration with Northwestern University; citizenship required. Write: Manager, Veterans Administration Hospital, Downey, near Waukegan, Illinois. C

WANTED—ONE OR TWO ADDITIONAL PSYCHIAtrists, ward physicians, for large county psychiatric hospital with qualified staff in southeastern medical center, university city; previous psychiatric training desirable, not mandatory; duties clinical, with some teaching; salary $6000 to $11,400 according to qualifications, with complete maintenance; vacations, sick leave, merit increases, retirement benefits. Write: Box 7992 C, % AMA.

GENERAL PRACTITIONER—TO JOIN ESTABLISHED eastern Ohio group of young specialists and general practitioners; enthusiastic, academic atmosphere; opportunity to become full partner from start with no investment; paid annual vacation and study period; starting annual salary $11,500-$15,000 depending on training and experience; retirement program. Box 7979 C, % AMA.

WANTED—ASSISTANT CHIEF ANAESTHESIOLOGY; 712 bed GM&S hospital, accredited for residency training; Board certification or qualification required; opportunities for teaching and research; salary range $11,355 to $12,770 plus 15% for Board Certification; liberal leave and attractive retirement program. Address inquiries to: Director, Professional Services, U. S. Veterans Administration Hospital, Oakland 12, California. C

PHYSICIAN WANTED—PHYSIATRIST PREFERRED; duties: Physician for intensive PM&R bed service in large Veterans Administration general hospital+ affiliated with Ohio State University Medical School; Board Certified Chief and excellent therapy staff; salary range $6,505-$13,970 depending on qualifications; also vacancy in 3 year PM&R residency. Write: Manager, Veterans Administration Center, Dayton, Ohio. C

WANTED—PHYSICIAN TO ASSOCIATE WITH SIX man group caring for mining company's employees and families; includes general practice, obstetrics, anesthesia, surgery and industrial work; salary $10,000 to start; no expenses; living conditions good; excellent schools; immediate opening. Call or write: N. W. Stewart, MD, Chief Surgeon, Homestake Hospital, Lead, South Dakota. C

MEDICAL STAFF DESIRES TO ATTRACT INTERNist, otolaryngologist, ophthalmologist and anesthesiologist to supplement existing specialties; growing community of 12,000; 50,000 in county; 120,000 in trade area, in south Illinois near Crab Orchard Lake; 6 year old hospital in planning expansion; send complete background and qualifications in first letter. Box 8017 C, % AMA.

WANTED—PEDIATRICIAN; BOARD CERTIFIED OR qualified to become third member of current two man pediatric department; varied and balanced pediatric practice; active teaching program; beautiful rural setting; salary; paid vacation; and excellent insurance program. Write: Dr. S. S. Morrison, Geisinger Memorial Hospital and Foss Clinic, Danville, Pennsylvania. C

OTOLARYNGOLOGIST WANTED—IF YOU ARE AN ear, nose and threat specialist, don't fail to write for particulars regarding the position which is now open for an otolaryngologist; this position offers the right man a chance to work in a busy office; excellent location; top notch salary; yearly advancement and early partnership. Reply at once to: Box 7993 C, % AMA.

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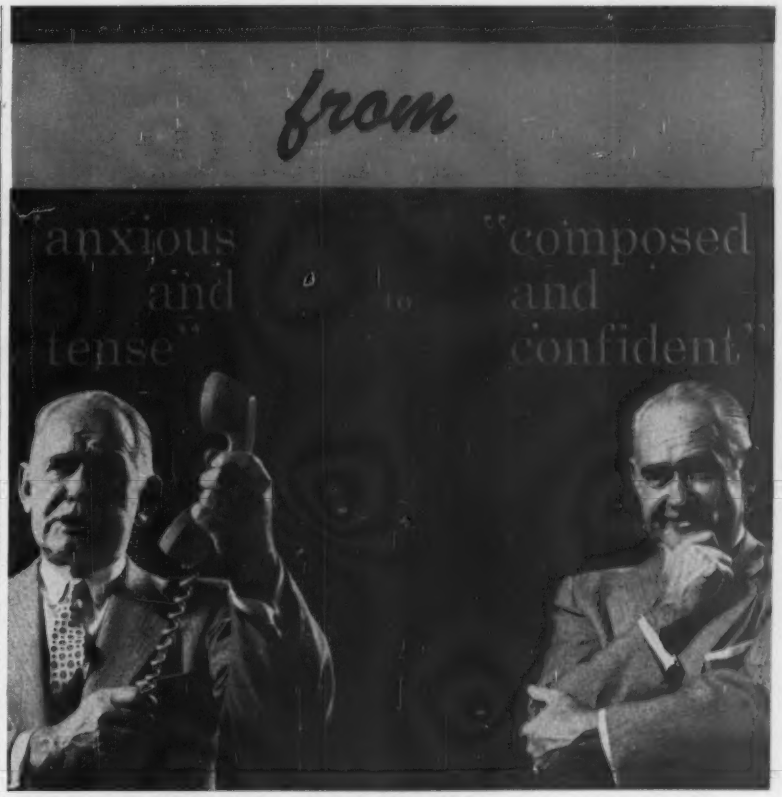

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TABLETS • REPEAT-ACTION TABLETS • ELIXIR • CAPSULES

1. Groesman, A. J.: Batterman, R. C., and Leifer, P.: Fed. Proc. 17:373 (March) 1958.

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MEDICAL ORGANIZATION HAS SALARIED POSItion for physician interested in working full time on permanent program of maintaining high standards of drug and other product advertising in reputable medical journals; some special training in internal medicine or pharmacology desirable; initial reply must include summary of personal and military background as well as references. Box 7370 C, % AMA.

PSYCHIATRISTS — NEUROLOGISTS; FULL TIME; part time; both treatment and examination positions; requirements; completion of residency; beginning salary $10,000-$14,700 depending on qualifications. Apply Varo #10, 128 N. Broad St., Philadelphia 2, Pa. Attention: Chief Neuropsychiatrist, LO 8-0400, Extension 140. C

GENERAL PRACTITIONER — CENTRAL NEW YORK State; established practice; dairy area; some industry; 6,000 people radius 8 miles; modern school; good roads; lake; golf; 25 bed community hospital in town; open staff, surgical privileges; home office combination, rent, purchase, easy terms; no investment; no charge for practice; specializing. Box 7939 C, % AMA.

WANTED—BOARD CERTIFIED ORTHOPEDIC SURgeon; for full time hospital practice in professional care program of the Miners Memorial Hospitals; starting compensation $20,000-$22,000; progressive pay scale. For details address: The Clinical Director, Miners Memorial Hospital Association, 1427 Eye Street, N. W., Washington, D. C. C

ANESTHESIOLOGIST—FOR 330 BED VETERANS ADministration general hospital; citizenship required; salary range $6,505 to $13,970 depending upon qualifications; plus 15% additional if board certified not to exceed $16,000; fringe benefits; board certified or board eligible preferred. Write: Manager, Veterans Administration Hospital, Muskogee, Oklahoma. C

PSYCHIATRIST — AN ATTRACTIVE OPENING EXists for a Board Certified or eligible doctor to join a clinic group in a middle west community; preferred age range 30 to 40 years; location is in a clean and desirable community of 50,000; substantial salary and association status will be negotiated; no investment required. Box 7943 C, % AMA.

WANTED — OTOLARYNGOLOGIST TO SERVE AS full time chief of section in 950 bed general hospital; U. S. citizenship required; Board Certified or eligible preferred; starting salary range up to $14,885 with sickness, retirement benefits, etc. Apply: Chief, Surgical Service, VA Hospital, East Orange, New Jersey. C

WANTED—INTERNIST; 254 BED GENERAL MEDICAL and surgical hospital; supervised by Board Certified physician and approved for preceptorship training; hospital located at home of University of Arkansas and in the heart of the Ozarks. Contact: Manager, Veterans Administration Hospital, Fayetteville, Arkansas. C

OPHTHALMOLOGIST — TO TAKE OVER A WELL established, active, high quality practice; excellent location in Portland, Oregon. Box 7974 C, % AMA.

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HOUSE PHYSICIANS—NEEDED JULY 1ST; 230 BED general hospital; serving suburban and industrial communities in Pittsburgh metropolitan area; must have Pennsylvania license; salary $650 per month; apartment available. Write: Administrator, Sewickley Valley Hospital, Sewickley, Pennsylvania. C

WANTED—GENERAL PRACTITIONER; EXCELLENT opportunity if qualified for Indiana license, also one primarily interested in obstetrics and pediatrics; in association with a group of 5 MD's doing a private and industrial practice; 25 miles south of Chicago Loop in the State of Indiana. Box 7459 C, % AMA.

WANTED — LUCRATIVE WESTERN INDIANA GENeral medical and surgical practice needs another well qualified MD to share load; new offices with good hospital facilities immediately available; good hunting and fishing; excellent country club; present MD 46 years of age; AAGP. Box 8023 C, % AMA.

WANTED—PSYCHIATRISTS; BOARD ELIGIBLE OR Certified; under 50 years of age; Deans Committee hospital 28 miles from Kansas City by turnpike; cost of living in area comparably less than elsewhere. Write: Director Professional Services, Veterans Administration Consolidated Center, Wadsworth, Kansas. C

WANTED—LICENSED HOUSE PHYSICIAN TO SUpervise emergency room for 185 bed general hospital in metropolitan Chicago. Box 7838 C, % AMA.

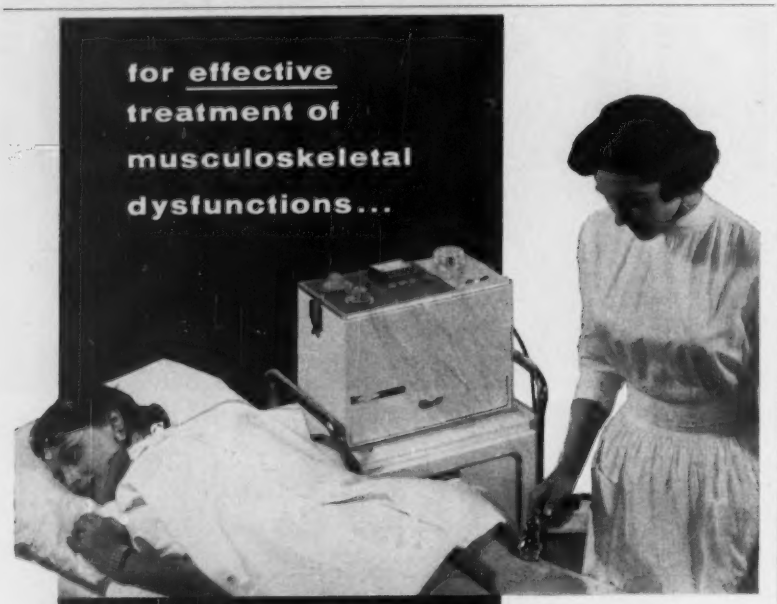
WANTED—GENERAL PRACTITIONER; UNDER 40; interested in internal medicine, to replace partner; well established practice, own building, fully equipped office; association without obligation on equal partnership basis; industrial community; Illinois; opposite St. Louis, Missouri. Box 7971 C, % AMA.

WANTED—PEDIATRICIAN; DIPLOMATE OR BOARD Eligible with service motive to join group of 10; college town, Allegheny foothills; new hospital with cobalt-60 teletherapy, radioisotope service, educational programs in surgery, nursing, laboratory and radiologic technology; early partnership. Box 7908 C, % AMA.

WANTED—PEDIATRICIAN AND OTOLARYNGOLOgist to start departments in a twenty member clinic with most of the specialties represented; central and new suburban division in large southern city; salary for three years then partnership if qualified. Box 7525 C, % AMA.

GENERAL PRACTICE FOR SALE—MARYLAND; ESTablished 10 years; well equipped office; complete files; low rent; gross over $25,000 last three years; hospital facilities for obstetrics, surgery; good location semi-rural area; practitioner over 35 best suited. Reply: Box 7996 C, % AMA.

STAFF PHYSICIAN — LARGE SOUTH-CENTRAL Tuberculosis Sanatorium; licensure necessary; salary range $7,560 to $9,120 depending upon experience; complete family maintenance, including modern 2 bedroom home. Box 7989 C, % AMA.



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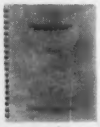

A new booklet of abstracts — "Ultrasonic Therapy — A Symposium" — is available without charge. Please address your request to the Burdick Corporation, Milton, Wisconsin.

WANTED — BOARD QUALIFIED INTERNIST WHO wishes to build private practice; to share office expenses with internist and two surgeons, share calls with internist; $12,000 guarantee plus percentage; north Iowa town; 30,000 shopping center for rich farming and industrial area. Box 7735 C, % AMA.

WANTED — INTERNISTS; BOARD CERTIFIED OR Board Eligible if well qualified; also vacancy in pulmonary tuberculosis; must be United States citizen; foreign graduates eligible if on approved list. Write: Manager, Veterans Administration Consolidated Center, Wadsworth (Leavenworth,) Kansas. C

WANTED — OBSTETRICIAN-GYNECOLOGIST; TO establish own practice; in office with established diplomate; Philadelphia area; references; training; state amount financial help needed for one year; permanent association if satisfactory or partnership. Box 7897 C, % AMA.

ORTHOPEDIC SURGEON; BOARD CERTIFIED OR qualified; to head department in well established 17 physician group in north midwestern college town of 50,000; new building; salary range $15,000 to $18,000; early partnership; send complete details. Box 8007 C, % AMA.

WANTED—BOARD CERTIFIED RADIOLOGIST; FOR full time hospital practice in professional care program of the Miners Memorial Hospitals; starting compensation $20,000; progressive pay scale. For details address: The Clinical Director, Miners Memorial Hospital Association, 1427 Eye Street, N.W., Washington 5, D. C. C

CERTIFIED PSYCHIATRIST — CERTIFICATION IN neurology also preferred; must be American graduate; interested in clinical work and helping teach residents; three year approved residency; salary to $22,800. Write: W. C. Brinegar, MD, Supt., Mental Health Institute, Cherokee, Iowa. C

INTERNIST—CERTIFIED OR QUALIFIED AS STAFF physician in 386 bed affiliated hospital; citizenship required; salary range $9,890 to $14,685; depending on experience or certification. Write: Director, Professional Services, Veterans Administration Hospital, Des Moines, Iowa. C

UNIVERSITY HEALTH PHYSICIAN POSITION available July 1; male doctor preferred; excellent diagnostic and th apeutic facilities; excellent growth and advancement ; ,ential; Cleveland-Akron area. Write to: Director, University Health Service, Kent State University, Kent, Ohio. C

GENERAL PRACTITIONER — YOUNG AND WELL trained to join active mixed group of 6 physicians; no obstetrics or surgery required; 35 miles from Chicago; $10,000 first year with bonus; early partnership. Box 7995 C, % AMA.

PATHOLOGIST—BOARD CERTIFIED OR ELIGIBLE; to join another in hospital clinical and tissue laboratory; near San Francisco; details training and experience first letter; adequate income; replies held confidential. Box 7679 C, % AMA.

GENERAL PRACTITIONER — INCLUDING OBSTETrics and surgery; excellent hospital facilities; good opportunity for right man; good income; south Florida east coast; Florida license required. Box 7914 C, % AMA.

GROUP IN PACIFIC NORTHWEST HAS OPENING for pediatrician; starting salary for Certified man, about $13,000; partnership within two years; For further information, contact: Dr. Peter L. Hurst, Permanente Clinic, 2606 N. E. Broadway, Portland, Oregon. C

HOUSE PHYSICIAN — COMMENCE DUTY JULY 1, 1959; 332 bed general hospital; minimum salary $500 per month; Pennsylvania license required. Write: Chairman, Resident-Intern Committee, St. Joseph's Hospital, Lancaster, Pennsylvania. C

OPHTHALMOLOGIST—BOARD QUALIFIED OR CERtified to head department in 12 man group in upper New York State; active established practice; new hospital optician on staff; partnership possible within three years. Box 7896 C, % AMA.

OBSTETRICIAN-GYNECOLOGIST UNIVERSITY trained, Certified, preferably academic affiliation; mature and experienced; to head division; midwest group of 17 certified members in various specialties; salary open. Send full particulars to: Box 7781 C, % AMA.

WANTED—ASSOCIATE IN EXCELLENT GENERAL medical and surgical practice in county seat town western Indiana; present associate likes this practice but likes husband better; husband wins; finances open. Box 8022 C, % AMA.

WANTED—CERTIFIED OR BOARD ELIGIBLE OBstetrician-gynecologist man to join a group of two who have a rapidly expanding practice in the twin cities of Minnesota; $12,000 to start; no investment with full partnership in five years. Box 7741 C, % AMA.

PEDIATRICIAN—BOARD ELIGIBLE; FOR MIDWEST university post in developmental pediatrics and infant neurology in teaching and research; salary and academic status dependent on training and experience. Box 7924 C, % AMA.

OTOLARYNGOLOGIST — URGENTLY NEEDED BY large southwest clinic group; Board Certified or Eligible for third ENT man; city of 175,000, rapidly expanding. Wire, phone, or write: Homer Reid, Lovelace Clinic, Albuquerque, New Mexico. C

CALIFORNIA MEDICAL BUREAU AGENCIES—FOR physicians placements and hospitals and medical properties for sale. 405 E. Green Street, Pasadena, California, and 610 S. Broadway Street, Los Angeles 14, California. C

INTERNIST—FORMAL TRAINING REQUIRED; MIDwest location 20,000 population near large city; five man group; complete x-ray and laboratory facilities; accredited hospital connections; $12,000 per year; early increase and association. Box 7806 C, % AMA.

INTERNIST — UNUSUAL OPPORTUNITY WITH large midwest pharmaceutical company; creative medical writing and clinical research; send full curriculum vitae; all correspondence confidential. Box 7666 C, % AMA.

PEDIATRICIAN-INTERNIST — BOARD QUALIFIED or Certified; full or part time for medical group in Staten Island; excellent opportunity; initial contract leading to partnership. Box 7984 C, % AMA.

PEDIATRICIAN WANTED—ESTABLISHED 14 MAN group in Indiana needs second man in department; Board qualified or Eligible; starting salary $15,000 with stable future practicing with well trained men. Box 7319 C, % AMA.

WANTED — GENERAL PRACTITIONER FOR ASSOciation in completely equipped clinic; suburb of Seattle; $1,000 per month with increase every six months for two years; then opportunity for partnership. Box 8011 C, % AMA.

GENERALIST—FOR SMALL OFFICE PRACTICE IN Bakersfield, California; ideal for older man desiring semi-retirement in desert climate; no investment. Write: L. O. Carpenter, MD, 910 Baker Street, Bakersfield, California. C

WANTED—GENERAL PRACTICE ASSOCIATE UNDER forty; with no military obligations; $1,000 a month; first 6 months; terms tailored to applicant's desires thereafter; send full particulars; including photo in first letter. F. A. Elders, MD, Cuba, Mo. C

OPHTHALMOLOGIST—UNIVERSITY TRAINED; CERtified; preferably academic affiliation; mature and experienced; to head division; midwest group of 17 Certified members in various specialties; salary open. Send full particulars to: Box 7981 C, % AMA.

PHYSICIAN WANTED—GENERALIST; LOCATE IN small town; will turn over large obstetric practice to qualified doctor; nothing for sale; doctor desires semi-retirement; 20 minutes to open staff hospital. Dr. Kirksey, Mulberry, Arkansas. C

WANTED—OBSTETRICIAN-GYNECOLOGIST; ESTABlished 14 man group in Indiana needs third man in department; Board Qualified or eligible; salary open above $12,000; excellent future practicing with well trained men. Box 8006 C, % AMA.

GENERAL PRACTITIONER—TO JOIN FIVE MAN modern clinic in college town; reference requested with application; salary $1,000 per month or 2/3 of gross income. Watson Clinic, Brookings, South Dakota. C

WANTED—ASSOCIATE, YOUNG; GENERAL PRACTItioner; rural 35,000; California license; beginning income adequate, immediate; no outlay to establish practice. Box 7910 C, % AMA.

WANTED — GENERAL PRACTITIONER FOR NEW York City suburbs; must be willing to work an honest $12,000 base salary plus percentage for two years then partnership. Box 7970 C, % AMA.

PATHOLOGIST — TO TAKE CHARGE OF DEPARTment; 225 bed hospital in New York State; arrangement open; furnish resume of experience. Box 7973 C, % AMA.

YOUNG PHYSICIAN LICENSED NEW YORK STATE interested in association with a group providing Board specialists in all fields; excellent opportunity for further education. Box 7985 C, % AMA.

DOCTORS—BOY SCOUT CAMP; NEW YORK STATE licensed; July and/or August; $400-$450 month plus room and board. Boy Scouts of America, 33 West 60th Street, New York 23, New York, Plaza 7-1905.

WANTED—ORTHOPEDIST; CERTIFIED OR BOARD Eligible; middle sized group in Illinois; salary open; early partnership; please give full details of qualifications and so forth. Box 7813 C, % AMA.

PEDIATRICIAN WANTED—TERRIFIC OPPORTUNITY for young man to work with pediatrician age 35 3-6 months, then take over growing practice in residential section of Brooklyn. Box 8013 C, % AMA.

GENERAL PRACTITIONER—TO TAKE OVER LUCRAtive practice northwestern Wisconsin town 8,000; excellent skiing, hunting, fishing; 2 open hospitals; ground floor office; clean, neat equipment. Box 8015 C, % AMA.

WANTED—UROLOGIST TO BECOME ASSOCIATED with a full time group, middle Atlantic States; give full qualifications and other particulars in first communication. Box 7906 C, % AMA.

WANTED — OTOLARYNGOLOGIST; BOARD CELTIfied or qualified; excellent offer in fine Massachusetts community. Write details including any experience in mobilization and tympanoplas to: Box 8024 C, % AMA.

INTERNIST — BOARD ELIGIBLE OR CERTIFIED; sub-specialty desired but not necessary; clinic specialty group in midwestern university city. Box 7991 C, % AMA.

WANTED—ANESTHESIOLOGIST TO JOIN PRESENT staff of three; Connecticut license necessary; Board Eligible; percentage with guaranteed minimum. Reply: Box 7886 C, % AMA.

EXCELLENT OPPORTUNITY FOR YOUNG MAN IN general practice of medicine in Colorado; salary first year of association; desirous of young married man. Reply to: Box 7768 C, % AMA.

INTERNIST—UNDER 45; IMMEDIATE OPENING IN small hospital-clinic in progressive Arizona mining community; salary about $900 per month; insurance program nets additional $600. Box 7915 C, % AMA.

OTOLARYNGOLOGIST—BOARD ELIGIBLE OR CERTIfied; as associate in private practice in growing suburban New York Community; good salary and early partnership. Box 7930 C, % AMA.

WANTED—ASSOCIATE PATHOLOGIST; EXPANDING institution; thirty minutes from Los Angeles; opportunity for teaching and research; salary $12,000 to $15,000 per year. If interested reply to: Box 7944 C, % AMA.

WANTED—PATHOLOGIST FOR JULY OR AUGUST; recently completed training or 4th year resident acceptable; 150 bed hospital eastern Illinois; good salary and car supplied. Box 7956 C, % AMA.

WANTED — INTERNIST BY WELL ESTABLISHED clinic in North Dakota; excellent facilities; early full partnership; professional and personal data requested in reply. Box 7958 C, % AMA.

PEDIATRICIAN—URGENTLY NEEDED BY EXPANDing group in Kentucky town of 25,000; early partnership. Box 7100 C, % AMA.

WANTED — FULL TIME INDUSTRIAL PHYSICIAN for transportation company; good salary and excellent working conditions. Address: Box 8003 C, % AMA.

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IOWA CITY — PSYCHIATRIC HESIDENCIES; DEpartment of Psychiatry, University of Iowa Medical Center; three year approved training; broad experience with adults and children; community services, inpatient and outpatient training and all types of psychiatric therapy under close supervision; Master of Science program for residents interested in academic and research careers; salary levels $5,600 to $4,200; also available "package plan" covering five years with periods of rotation in the Department of Psychiatry and the state mental hospitals and schools for mentally defectives; salary levels $6,750 to $9,150. For information and application blanks, write: Paul E. Huston, MD, Chairman, Department of Psychiatry, 500 Newton Road, Iowa City, Iowa. D

RESIDENT—GENERAL SURGERY; CHIEF SURGEON in supervised residency in 3,500 bed mental hospital integrated with approved residency in 250 bed general hospital; $585 month; available July 1, 1959; 2 years approved residency or equivalent required. Write: W. C. Perdew, DD, Administrator, Bronson Methodist Hospital, Kalamazoo, Michigan. D

INTERNSHIPS—175 BED GENERAL HOSPITAL; EXcellent educational programs, seminars, clinics and conferences; all services; teaching staff, wonderful opportunity; salary $100 per month, first three months; $125 per month, second three months and $150 per month thereafter; two weeks vacation; hospital fully approved by Joint Commission on Accreditation; full maintenance. Walther Memorial Hospital, Chicago 51, Illinois. D

RADIOLOGY — THIRD YEAR RESIDENCY OPEN beginning January 1, 1960; stipend $300 plus room and board; active general hospital on eastern seaboard; department is staffed by three full time radiologists, physicist, and connected with medical school; only those with 2 years of good training need apply; state all particulars in first letter. Box 8030 D, % AMA.

RESIDENT—GENERAL SURGERY; 231 BED General hospital; 2nd year of 3 year approved clinical program; university affiliation; $340 month; no maintenance; one year approved residency or equivalent required; available July 1, 1959. Write: W. C. Perdew, DD, Administrator, Bronson Methodist Hospital, Kalamazoo, Michigan. D

RESIDENCY IN RADIOLOGY FOR JANUARY 1, 1960; active medical-surgical hospital in large city on eastern seaboard; connected with medical school; three full time radiologists; physicist; training includes cobalt and isotopes. Box 8031 D, % AMA.

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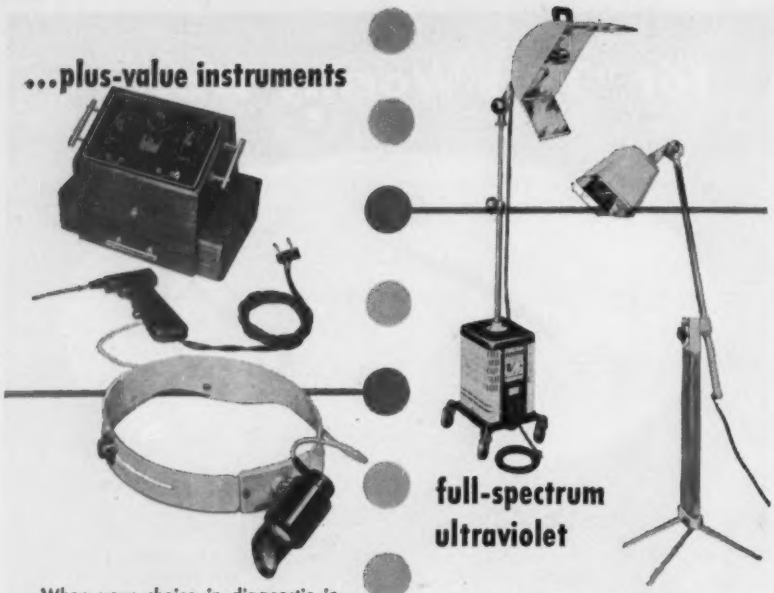

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(Continued from preceding page)

PATHOLOGY RESIDENCIES AVAILABLE FOR JULY 1, 1959, 4 year approval for anatomical and clinical pathology; affiliated with Marquette University program; stipend ranges: $3,250 to $4,945 a year; U. S. citizenship required. Write: Chief, Laboratory Service, Veterans Administration Center, Wood, Wisconsin. D

CHIEF RESIDENT FOR JULY 1ST APPOINTMENT to two year general practice program approved by AMA and Department of State for Exchange Visitors; general hospital treating men, women and children; good salary; graduate of approved school desired; explain in detail training and experience. Apply: Administrator, Woman's Hospital, 1940 East 101st Street, Cleveland 6, Ohio. D

EXCELLENT GENERAL ROTATING RESIDENCY IN 126 bed general hospital; Philadelphia suburbs; $300 per month plus full maintenance; no exchange visitor number. Apply: Delaware County Hospital, Drexel Hill, Pennsylvania. D

WANTED — ROTATING INTERNS; APPROVED 400 bed general hospital in federal psychiatric hospital; annual stipend $3,100. Apply to: Winifred Overholser, MD, Superintendent, Saint Elizabeth's Hospital, Washington, D. C. D

WANTED—JULY 1, 1959; RESIDENT PHYSICIAN; railroad hospital, Indiana town of 15,000 population; good salary; applicants must qualify for Indiana license. Apply: Box 8048 D, % AMA.

SURGICAL RESIDENTS—FIRST AND SECOND YEAR, approved 3 year program, for graduates of approved medical schools or foreign who have passed ACFMG; beginning remuneration if married; $5,400, plus perquisites. Write: Chief of Surgery, Harlan Memorial Hospital, Harlan, Kentucky. D

FULLY APPROVED CAREER AND REGULAR RESIDencies in physical medicine and rehabilitation available for one to three years; salary range $3,250 to $9,890. Apply: Chief, Physical Medicine and Rehabilitation Service, Veterans Administration Hospital, Bronx 68, New York. D

ANESTHESIA—SPECIALIZED TRAINING IN ANESthesia offered to second or third year residents; experience in open-heart, aortic grafts, hypothermia as well as anesthetic management of other formidable surgery. Apply: Director of Education, Cleveland Clinic Foundation, 2020 East 93rd Street, Cleveland 6, Ohio. D

GENERAL PRACTICE RESIDENCY — AVAILABLE July 1, 1959; fully accredited by JCAH; closely affiliated with well known midwestern clinic; only graduates of approved medical schools or ECFMG Certified will be considered; salary $500 per month; excellent opportunities for future. Apply: Box 8029 D, % AMA.

ALLERGY RESIDENT — JULY, 1959; APPROVED; training medicine or pediatrics required; Certification Council Foreign Graduates required. Medical College of Virginia, apply: M. E. B. Owens, MD, 1001 West Franklin Street, Richmond, Virginia. D

NEW YORK CITY—RESIDENTS; A PSYCHIATRIC service in a general hospital with approved three year training program; all para-medical services fully operative, located in the Greenwich Village section of New York City; physical plant modern, up-to-date, recently constructed; this general hospital consists of 830 beds covering all specialties, and including a current capacity of 33 beds in a psychiatric pavilion; affiliated with New York University-Bellevue Medical Center; residencies available at 1st and 3rd year levels. For further information, write: The Administrator, St. Vincent's Hospital*+ of the City of New York, 153 W. 11th Street, New York 11. Applications now being accepted for training year starting July 1, 1960. D

INTERNSHIP, ROTATING: AVAILABLE JULY 1, 1959, in approved 500 bed county charity hospital; teaching provided by active volunteer visiting staff of over 150 Board or Board eligible physicians; 1 and 2 bedroom furnished apartments available at $10 per month together with laundry and 3 meals per day; stipend $250 per month; malpractice insurance furnished; inquiries are invited from foreign students who have successfully completed the American Medical qualification examination given by the Educational Council for foreign medical graduates. For information contact: Superintendent, San Bernardino County Charity Hospital*+, 780 East Gilbert Street, San Bernardino, California. D

APPROVED THREE YEAR RESIDENCIES IN PSYchiatry; new GM&S hospital; well organized teaching program; affiliated with Washington University School of Medicine; all types of psychiatric experience represented, including supervised dynamically oriented psychotherapy, psychosomatic medicine, child guidance, etc.; approved training in psychoanalysis available locally; full time director of training is a member of the American Psychoanalytic Association; attractive career residency program available; citizenship required. Write to: Dr. Bernard A. Cruvant, Veterans Administration Hospital, 915 North Grand Avenue, St. Louis 6, Missouri. D

WANTED—PATHOLOGY RESIDENT; 250 BED GENeral hospital, Pacific northwest; close association with pathologist certified in clinical pathology and pathologic anatomy; also with chemist and bacteriologist; emphasis on training program in all branches includ.ng both academic and practical approach; 5,000 surgical tissues, 200 autopsies and 150,000 clinical tests annually; training in AMA approved school required or applicant must have passed AMA Intern Qualifying Examination; attractive outdoor recreational facilities include water skiing, fishing, hunting and snow skiing, salary open. Write: Ted E. Ludden, MD, Pathologist, Deaconess Hospital, Spokane, Washington. D

APPROVED RESIDENCY; PATHOLOGIC ANATOMY and Clinical Pathology—four year program currently six residents; two vacancies for July 1, 1959; permanent staff of two board certified Pathologists; MD Hematologist; chemist; Microbiologist; technical staff about 40; in 1958; 10,868 surgical tissues; 395 autopsies; total examinations 591,603. Stipend 1st year $4,200, second $4,500, third $4,800, fourth $5,400. Explain in detail education and training; apply John J. Clemmer, MD, Bender Laboratory Hospitals, 136 St. Lake Avenue, Albany 8, N. Y. D

RESIDENCIES—MENNINGER SCHOOL OF PSYCHIAtry; approved three year program; balanced clinical and didactic training including psychotherapy and somatic therapies; out-patient and child physchiatry; at Veterans Administration, State and Menninger Hospitals; affiliated with Topeka Institute for psychoanalysis; five year appointments combining residency and staff experience for Board Eligibility available at staff salaries. Write: Registrar, Menninger School of Psychiatry, Topeka, Kansas. D

WANTED — ONE FIRST YEAR RESIDENT IN PAthology for July 1, 1959; graduate of U. S. or Canadian Class A medical school; 300 bed modern hospital with active graduate training program; full 4 year approval in P.A. and C.P.; 2 full time board pathologists; 2 board consultants; biochemist; microbiologist; topnotch progressive laboratory; 5042 surgicals and 165 autopsies in 1958; stipend $375.00; contact director of laboratories, McLaren General Hospital, Flint, Michigan. D

PATHOLOGY — CALIFORNIA; 1,500 BED HOSPITAL fully approved for 4 years training in clinical pathology and pathological anatomy; one vacancy exists in career resident program offering full staff pay ranging from $6,505 to $9,890 dependent on qualifications; complement of 8 residents supervised by four full time Certified pathologists with university affiliations. Write: Director, Professional Services, Veterans Administration Hospital, Long Beach 4, California. D

VACANCIES—SENIOR PHYSICIANS WITH MINIMUM of three years psychiatric experience; excellent opportunities for advancement; salary rate $7320-$10,200 depending upon applicant's training and experiences; annual increments; nominal deduction for complete family maintenance; fully approved large eastern mental hospital*+ with 3 year accredited residence training progress; must be eligible for licensure in Connecticut. Box 7977 D, % AMA.

RESIDENCIES — INTERNAL MEDICINE; 1,300 BED general hospital*+; 3 year; Baylor University College of Medicine affiliation; includes all specialties under supervision of Board Certified specialists; $3,250 to $4,945; must be graduate of United States or Canadian medical school; appointments available for 1960. H. D. Bennett, MD, Veterans Administration Hospital, Houston, Texas. D

STAFF PSYCHIATRISTS AND RESIDENTS—GRACIE Square Hospital; a new 232 bed private psychiatric hospital in midtown Manhattan has complete psychiatric; medical and surgical facilities for active treatment of all psychiatric disorders; appointments in all categories immediately available; first year residents start $4,000. Write: Leonard Cammer, MD, Director, 420 East 76th Street, New York 21, N. Y. D

WANTED—GENERAL HOUSE PHYSICIAN AVAILable July 1, 1959; 313 beds and 36 bassinets; fully accredited by JCAH; approved for intern training; surgical and pathological residencies; only graduates of approved medical schools of United States and Canada will be considered; salary plus maintenance. Apply: The Administrator, The Williamsport Hospital*+, Williamsport, Pennsylvania. D

ROTATING INTERNSHIPS OF ONE YEAR AVAILable—New wing to be opened this summer bringing hospital*+ to 500 beds; new surgery; x-ray; outpatient departments; stipend $125 per month plus maintenance. Methodist Hospital, Peoria, Illinois. D

(Continued on page 250)

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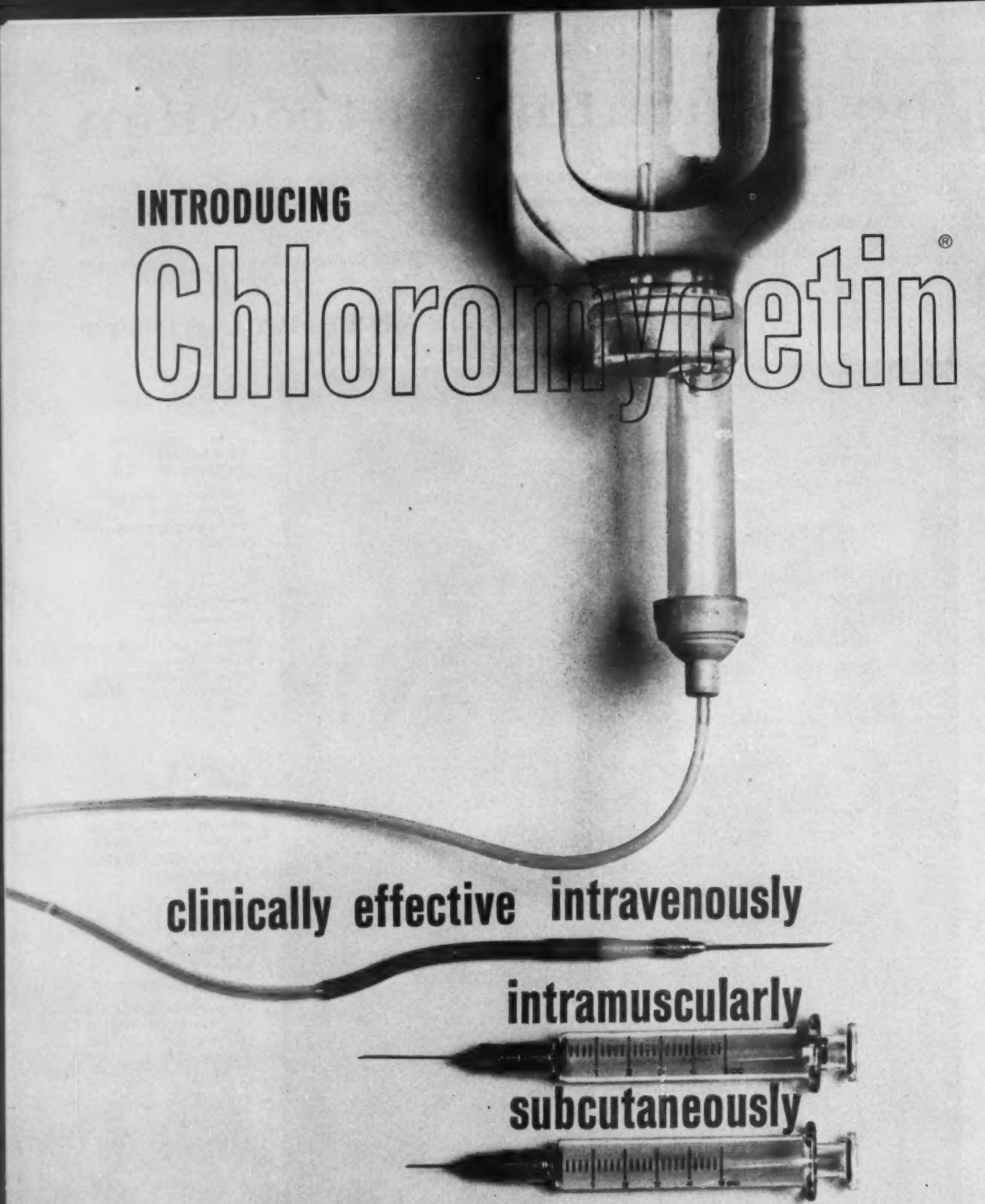

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TYPICAL CLINICAL EXPERIENCE WITH CHLOROMYCETIN SUCCINATE

Type of infection	Number of Patients	RESULTS Excellent to Good	Fair	Poor
Respiratory[1,3*]	32	32		
Shigella dysentery[1]	14	14		
Enteritis[1]	10	6	2	2
Bacteremia[3,4]	5	5		
Meningitis[1,4]	4	3		1**
Rocky Mountain spotted fever[1,4]	2	2		
Ear abscess with cellulitis[3]	1	1		
Lung abscess[3]	1			1
Typhoid fever[4]	1	1		
TOTALS	70	64	2	4

*Includes 15 patients who were administered CHLOROMYCETIN SUCCINATE by nebulization under intermittent positive pressure breathing.

**Patient was hydrocephalic at birth; cerebrospinal fluid was sterile at time of death.

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CHLOROMYCETIN SUCCINATE is well tolerated, even by small children. Signs of irritation at injection sites have been few.[1-4]

DOSAGE AND ADMINISTRATION—*Adults:* 1 Gm. every six to eight hours. *Children:* 100 mg. per Kg. of body weight per day in divided doses at six- to eight-hour intervals. The total dose in children should not exceed the adult dose of 1 Gm. given at any single injection, with exception of treatment of *Hemophilus influenzae* meningitis in which higher doses are employed.

In all cases, severity of infection and clinical response to therapy should be the guiding factors determining the proper dosage schedule. Premature and full-term newborn infants require special dosage supervision. For details see literature.

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REFERENCES—(1) Ross, S.; Puig, J. R., & Zaremba, E. A., in Welch, H., & Marti-Ibañez, F: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 803. (2) Glazko, A. J., *et al.*: *ibid.*, p. 792. (3) Payne, H. M., & Hackney, R. L., Jr., in Welch, H., & Marti-Ibañez, F: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 821. (4) McCrumb, F. R., Jr.; Snyder, M. J., & Hicken, W. J.: *ibid.*, p. 837.

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— Rein, C. R., and Fleischmajer, R.: Personal Communication.

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(Continued from page 246)

RADIOLOGY RESIDENCY—THREE YEAR APPROVED program in 1,500 bed general hospital; affiliated with Baylor University College of Medicine, Texas Medical Center; complete training in diagnosis, therapy, including supervoltage, and radioisotopes; must be U. S. citizens or graduate of U. S. or Canadian medical schools. Manager, Veterans Administration Hospital+, Houston, Texas. D

ROTATING INTERNSHIPS—APPROVED; AVAILABLE immediately; 375 bed hospital active teaching program; member exchange visitor program; candidates must be able to speak English fluently; stipend $200.00 per month plus full maintenance; apply: Chairman, Resident-Intern Committee, West Suburban Hospital, 518 North Austin Blvd., Oak Park, Illinois. D

RESIDENTS—GENERAL ONE YEAR ROTATING RESidency starting July 1, 1959 in accredited 174 bed general hospital; attractive mountain, seaside, resort city; United States citizenship; one year internship and eligibility for California license required; salary $560 per month. Apply: Director, County Hospital, Santa Cruz, California. D

INTERNSHIPS AVAILABLE—12 MONTHS ROTATING general including isotope, electroencephalogram and research laboratories; salary $250 per month plus full maintenance for single interns; some apartments available for married interns. Apply: Chairman, Resident-Intern Committee, St. Joseph's Hospital*+, Lancaster, Pennsylvania. D

ANESTHESIOLOGY RESIDENCIES — APPROVED 2 year active teaching program with unusually wide clinical experience; opportunities for clinical, teaching and research appointments in hospital and medical college after completion of training. Write: C. M. Landmesser, MD, Director of Anesthesiology, Albany Medical Center*+, Albany, New York. D

UROLOGY RESIDENCY—BECAUSE OF UNEXPECTED vacancy for July; applications are currently being considered for appointment to the first (general surgery) year of our approved 4 year program; no pyramid; must be licensed or eligible for license in Illinois. If interested apply to Medical Director, Michael Reese Hospital*+, Chicago 16. D

APPROVED ROTATING INTERNSHIPS — 485 BED general hospital associated with medical school; excellent teaching program; approved for complete residency training in medicine, surgery, obstetrics and gynecology, radiology, pathology, and anesthesiology; salary $175; graduates of approved schools or ECFMG certification only. Box 7836 D, % AMA.

ANESTHESIOLOGY RESIDENCY — VANDERBILT University Hospital*+; approved 2 year didactic and clinical program; an opening every October, January, April and July; maintenance plus beginning stipend of $183 per month. Address: Benjamin H. Robbins, MD, Professor of Anesthesiology, Vanderbilt University School of Medicine, Nashville, Tennessee. D

1 AND 2 YEAR GENERAL PRACTICE RESIDENCIES; 1 year residencies in general surgery; available July 1, 1959; graduates U. S. and Canadian medical schools; monthly salary $440; housing AMA approved. Apply: Chief of Professional Services, General Hospital, Riverside County, Arlington, California. D

POSITION AVAILABLE FOR APPROVED ROTATING internship; 400 bed general hospital*+; extensive teaching program; approved residency; $250 per month, maintenance, $50 living expenses for married interns. Inquire: Director of Medical Education, Providence Hospital, Seattle, Washington. D

WANTED—FOR JULY 1ST FOR SOUTHERN HOSpital two junior assistant residents for fully approved four year surgical program with rotation through surgical specialties; applicants from approved schools desired; beginning stipend $2,400 increasing to $3,600 for fourth year; full maintenance. Box 7898 D, % AMA.

PATHOLOGY RESIDENCY — APPROVED 250 BED hospital in Brockton, Massachusetts; 23 miles from Boston; one day a week spent in Boston at teaching hospital; $250.00 per month plus maintenance; contact: Chief of Pathology, Brockton Hospital, Brockton, Mass. D

ANESTHESIOLOGY RESIDENCIES—AT UNIVERSITY of Minnesota Hospitals, Minneapolis Veterans Administration Hospitals and associated hospitals; an opening every 4 weeks. Address: Frederick H. Van Bergen, MD, Director of Anesthesiology, University of Minnesota Hospital, Minneapolis, Minnesota. D

DERMATOLOGY—SECOND AND THIRD YEAR RESIdencies integrated teaching program leading to MS or DS degrees from Temple University; $100 per month with full maintenance. C. F. Burgoon, Medical Director, Skin and Cancer Hospital of Philadelphia+, Unit. Dept. of Dermatology, Temple University. D

WANTED—GENERAL PRACTICE RESIDENTS; 150 bed general hospital located in beautiful coastal community of 65,000; year round recreational activities; salary $600 per month; to begin July 1, 1959; must be U. S. citizen. Write to: Administrator, San Luis Obispo General Hospital, San Luis Obispo, California. D

APPROVED ROTATING INTERNSHIPS, 1959 TO 1960, in 196 bed general hospital; stipend $200 monthly; full maintenance; active program. Russell Tyler, MD, Santa Fe Hospital, 610 South St. Louis Street, Los Angeles, California. D

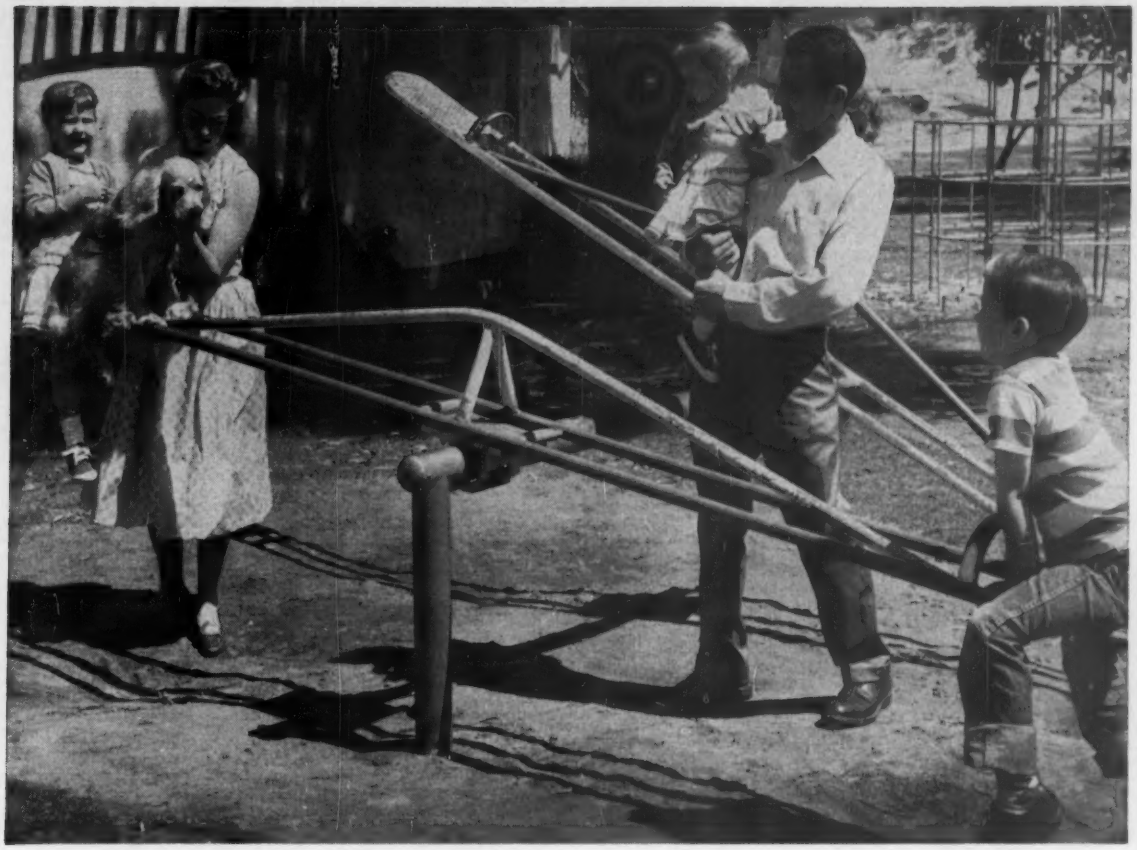
1 YEAR ROTATING INTERNSHIPS; AVAILABLE July 1, 1959; graduates U. S. and Canadian medical schools; monthly salary $314; housing AMA approved. Apply: Chief of Professional Services, General Hospital*+, Riverside County, Arlington, California. D

RESIDENT PHYSICIAN—100 BED GENERAL HOSpital; near Boston; good salary; apartment for family; position available July 1, 1959; must be United States citizen or permanent resident. Write: Administrator, Symmes Hospital, Arlington 74, Massachusetts. D

RADIOLOGY RESIDENCY—THREE YEAR APPROVED program in eastern medical school, hospital 1,000 beds; $200 first, $225 second, $250 third year, plus full maintenance. Reply with all details in first letter. Box 7812 D, % AMA.

PATHOLOGY RESIDENTS — EXPANDING INSTITUtion; thirty minutes from Los Angeles; $4,800 per annum. Box 7972 D, % AMA.

(Continued on page 257)



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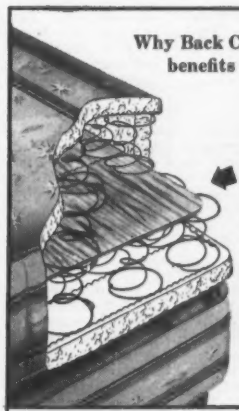

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BOOKS RECEIVED

Books received by THE JOURNAL *are acknowledged in this column. Selections will be made for more extensive review in the interests of* THE JOURNAL *readers as space permits. Books listed in this department are not available for lending or sale through the American Medical Association.*

Die Gefässarchitektur der Niere: Untersuchungen an der Hundeniere. Von Prof. Dr. A. von Kügelgen, Dr. B. Kuhlo, Dr. W. Kuhlo und Dr. Kl.-J. Otto. Mit einem Vorwort von Prof. Dr. S. Janssen, Direktor des Pharmakologischen Instituts der Universität Freiburg i.Br., und einer physiologischen Einführung von Doz. Dr. G. Grupp. Heft 5, Zwanglose Abhandlungen aus dem Gebiet der normalen und pathologischen Anatomie. Herausgegeben von Prof. Dr. W. Bargmann, Direktor des Anatomischen Instituts der Universität Kiel, und Prof. Dr. W. Doerr, Direktor des Pathologischen Instituts der Universität Kiel. Paper. 47 marks; $11.20. 37.60 marks; $8.85 subscription price. Pp. 111, with 89 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

Gynecology and Gynecologic Nursing. By Norman F. Miller, M.D., Professor of Obstetrics and Gynecology, University of Michigan Medical School, Ann Arbor, and Hazel Avery, A.B., R.N., Associate Professor of Nursing and Supervisor, Obstetric and Gynecologic Nursing, University of Michigan Medical Center. With chapter on gynecology operating room by Mildred Quackenbush, B.S.N.Ed., R.N., Assistant Professor of Nursing, and Supervisor of Operating Rooms, University of Michigan Medical Center, and chapter on psychosomatic approach in gynecology by Sprague Gardiner, M.D., Professor of Obstetrics and Gynecology, University of Michigan Medical Center. Fourth edition. Cloth. $5.50. Pp. 501, with 249 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Textbook of Physiology and Biochemistry. By George H. Bell, B.Sc., M.D., F.R.F.P.S.G., Professor of Physiology in University of St. Andrews at Queen's College, Dundee, J. Norman Davidson, M.D., D.Sc., F.R.F.P.S.G., Gardiner Professor of Biochemistry in University of Glasgow, Glasgow, and Harold Scarborough, M.B., Ph.D., F.R.C.P.E., Professor of Medicine in Welsh National School of Medicine of University of Wales, Cardiff. With foreword by Robert C. Garry, M.B., D.Sc., F.R.F.P.S.G., Regius Professor of Physiology in University of Glasgow. Fourth edition. Cloth. $12.50. Pp. 1065, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

Morbidity from Cancer in the United States. Part I: Variation in Incidence by Age, Sex, Race, Marital Status and Geographic Region. Part II: Trend in Morbidity, Association with Income and Stage at Diagnosis. By Harold F. Dorn, Ph.D., and Sidney J. Cutler, M.A. U. S. Department of Health, Education, and Welfare, Public Health Service. Public health monograph no. 56. Public Health Service publication no. 590. Issued concurrently with January 1959 issue of Pub. Health Rep., vol. 73, no. 12. Part I published separately in 1955 as public health monograph no. 29, Public Health Service publication no. 418. Paper. $1. Pp. 207, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1959.

Childbearing Before and After Thirty-five: Biologic and Social Implications. By Dr. Adrien Bleyer. Statistical study of favored—and less favored—years for human procreation. Book planned for college students and leaders of society who will show the way; the commonalty will follow, according to their lights. Introduction by Dr. Richard L. Jenkins, Director, Psychiatric Evaluation Project, U. S. Veterans Administration, Washington, D. C. Commentary by Dr. Douglas P. Murphy, Associate Professor of Obstetrics and Gynecology, Gynecean Hospital Institute, University of Pennsylvania, Philadelphia. Cloth. $2.95. Pp. 119, with illustrations. Vantage Press, Inc., 120 W. 31st St., New York 1, 1958.

The Trial of Dr. Adams. By Sybille Bedford. Half cloth. $3.75. Pp. 245. Simon & Schuster, Inc., 630 Fifth Ave., Rockefeller Center, New York 20, 1958.

Diffuse Lesions of the Stomach: An Account with Special Reference to the Value of Gastric Biopsy. By Ian J. Wood, M.D., F.R.C.P., F.R.A.C.P., Assistant Director of Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital, Melbourne, Victoria, Australia, and Leon I. Taft, M.B., B.S., B.Sc., Pathologist to Clinical Research Unit of Royal Melbourne Hospital. Cloth. $6. Pp. 86, with 35 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-43 Maddox St., London, W. 1, England, 1958.

Community College Education for Nursing: An Experiment in Technical Education for Nursing. Report of the Cooperative Research Project in Junior-Community College Education for Nursing. By Mildred L. Montag, Ed.D., Professor of Nursing Education, Teachers College, Columbia University, New York. Part II by Lassar G. Gotkin, Ed.D. Cloth. $6. Pp. 437. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1959.

A History of Neurology. By Walther Riese, M.D., Associate Professor of Psychiatry and Neurology, Medical College of Virginia, Richmond. Foreword by Félix Martí-Ibáñez, M.D., Professor and Director of Department of History of Medicine, New York Medical College, Flower & Fifth Avenue Hospitals, New York. MD monographs on medical history, number two. Under editorial direction of Félix Martí-Ibáñez, M.D. Cloth. $4. Pp. 223. MD Publications, Inc., 30 E. 60th St., New York 22, 1959.

Colorimetric Determination of Traces of Metals. By E. B. Sandell, Ph.D., Professor of Analytical Chemistry, University of Minnesota, Minneapolis. Chemical Analysis, volume III. Series of monographs on analytical chemistry and its application. Editors: Beverly L. Clarke, P. J. Elving and I. M. Kolthoff. Third edition. Cloth. $24. Pp. 1032, with 110 illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publisher, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1959.

Radiographic Atlas of Skeletal Development of the Hand and Wrist. By William Walter Greulich, Professor of Anatomy, Stanford University School of Medicine, Stanford, Calif., and S. Idell Pyle, Research Associate, Departments of Anatomy, Western Reserve University, Cleveland, and Stanford University Schools of Medicine. Second edition. Cloth. $15. Pp. 256, with illustrations. Stanford University Press, Stanford, Calif.; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England, 1959.

The Anatomy of the Nervous System: Its Development and Function. By Stephen Walter Ranson, M.D., Ph.D. Revised by Sam Lillard Clark, M.D., Ph.D., Professor and Chairman of Department of Anatomy, Vanderbilt University School of Medicine, Nashville. Tenth edition. Cloth. $9.50. Pp. 622, with 434 illustrations. W. B. Saunders Company, W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Die Entfremdungserlebnisse: Über Herkunft und Entstehungsweisen der Depersonalisation. Von Prof. Dr. Joachim-Ernst Meyer. Sammlung psychiatrischer und neurologischer Einzeldarstellungen. Herausgegeben von K. Conrad, W. Scheid, und H. J. Weitbrecht. Paper. 12.60 marks; $3. 11.35 marks; $2.70 subscription price. Pp. 64. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

Experimentation in Man. By Henry K. Beecher, M.D. Publication number 352, American Lecture Series, monograph in American Lectures in Medicine. Reprinted from Journal of American Medical Association. Cloth. $3.50. Pp. 80. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, [1959].

The Mentally Retarded Child at Home: A Manual for Parents. By Laura L. Dittmann. U. S. Department of Health, Education, and Welfare, Social Security Administration, Children's Bureau. Children's Bureau publication no. 374. Paper. 35 cents. Pp. 99, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1959.

Recent Advances in Respiratory Tuberculosis. By Frederick Heaf, *C.M.G.*, M.A., M.D., David Davies Professor of Tuberculosis, Welsh National School of Medicine, Cardiff, and N. Lloyd Rusby, M.A., D.M., F.R.C.P., Physician to London Hospital, London. Fifth edition. Cloth. $8. Pp. 284, with 20 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

An Analysis of Language Development in Children with Impaired Hearing. By William G. Hardy, Miriam D. Pauls, and Harriet L. Haskins. Research project of Johns Hopkins School of Hygiene and Public Health, undertaken by grant in aid from U. S. Public Health Service, B-773. Acta otolaryng., supp. 141. Paper. Pp. 51, with 5 illustrations. Acta oto-laryngologica P. O. B. 400, Uppsala, Sweden, 1958.

Gutachten des Bundesgesundheitsamtes über die Durchführung des Impfgesetzes: Unter Berücksichtigung der bisherigen Erfahrungen und neuer wissenschaftlicher Erkenntnisse. Abhandlungen aus dem Bundesgesundheitsamt, Heft 2. Paper. 27 marks. Pp. 171, with 6 illustrations. Springer-Verlag, Heidelberger Platz 3, (1) Berlin-Wilmersdorf (West Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1959.

Ten Years of Progress with Exceptional Children 1947-1957: Education Special. Annual publication, Hunter College chapter, International Council for Exceptional Children, volume X, number one. Special tenth anniversary issue. Paper. $1; discount for quantity orders. Pp. 88, with illustrations. International Council for Exceptional Children, Hunter College chapter, 695 Park Ave., New York 21, 1957.

Help for Ten Million: A Manual for Patients with Arthritis, Rheumatism and Gout. By Darrell C. Crain, M.D., F.A.C.P., Clinical Associate Professor in Medicine, Georgetown University Medical School, Washington, D. C. Keystone books in medicine K5, under general editorship of Edward S. McCabe, M.D. Paper. $1.45. Pp. 251, with 13 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5, 1959.

The Hand: Its Anatomy and Diseases. By John J. Byrne, M.D., Director, Third (Boston University) Surgical Service and Research Laboratory, Boston City Hospital, Boston. Cloth. $10.50. Pp. 384, with 166 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

Selected Materials on Environmental Aspects of Staphylococcal Disease: C D C Training Program. U. S. Department of Health, Education, and Welfare, Public Health Service, Bureau of State Services, Communicable Disease Center, Atlanta, Georgia. Public Health Service publication no. 646. Paper. Pp. 289, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1959.

The Plasma Proteins: Clinical Significance. By Paul G. Weil, B.A., M.D.C.M., M.Sc., Director, Transfusion Service and Assistant Physician, Royal Victoria Hospital, Montreal. Material published in American Practitioner & Digest of Treatment, September 1958. Cloth. $3.50. Pp. 133, with 2 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1959.

The Ecology of Human Disease. By Jacques M. May, M.D., Director, Medical Geography Department, American Geographical Society, New York. Foreword by Felix Martí-Ibáñez, M.D., Professor and Director, Department of History of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, New York. Cloth. $7.50. Pp. 327, with illustrations. MD Publications, Inc., 30 E. 60th St., New York 22, 1958.

Low-Fat Diet: Reasons, Rules, and Recipes. By Roy L. Swank, M.D., Professor and Head of Division of Neurology, Department of Medicine, University of Oregon Medical School, Portland, and Aagot Grimsgaard, Research Associate, Division of Neurology, University of Oregon Medical School. With technical assistance of Roberta Lee Penny. Paper. $2.50. Pp. 143. University of Oregon Books, Eugene, 1959.

(Continued on page 257)

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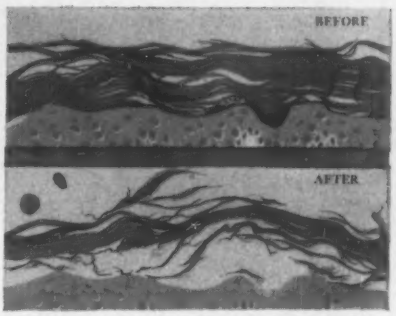

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REFERENCES: 1. Flesch, P.: Proceedings Scientific Session. Toilet Goods Assoc. June, 1958. 2. Samitz, M. H.: Ann. New York Acad. Sc. 73:1020, 1958. 3. Flesch, P., and Jackson Esoda, E. C.: Ann. New York Acad. Sc. 73:989, 1958. 4. Bleiberg, J., and Saltzman, J. A.: Clin. Med. 5:485, 1958. 5. Bleiberg, J.: Ann. New York Acad. Sc.: 73:1028, 1958. 6. Clyman, S. G.: Ann. New York Acad. Sc. 73:1032, 1958. 7. Welsh, A. L., and Ede, M.: Ohio M. J.: to be published.

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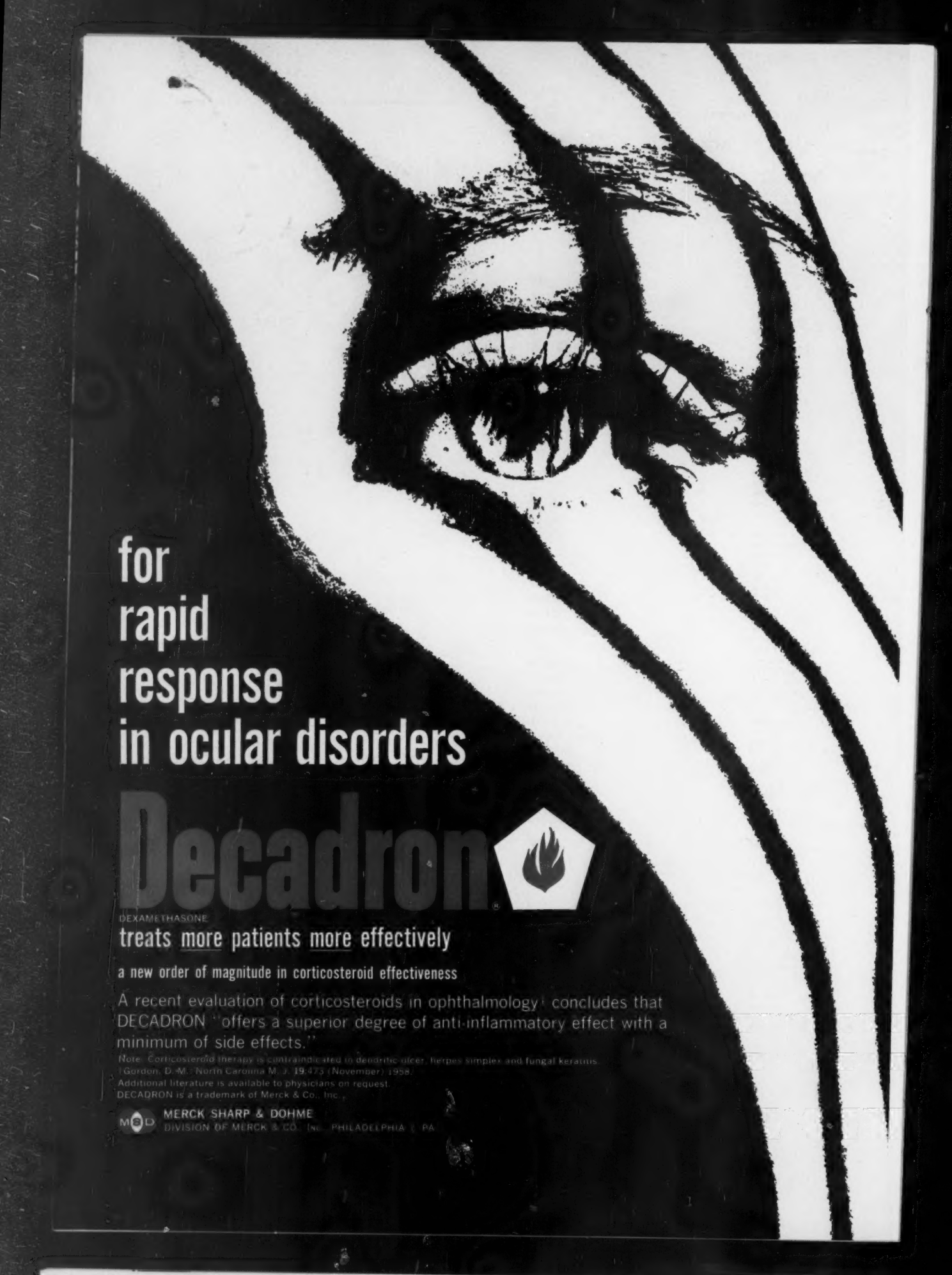
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[1] Gordon, D. M.: North Carolina M. J. 19:473 (November) 1958.
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(Books Received Continued)

The Clinical Examination of Patients with Organic Cerebral Disease. By R. Klein, M.D., and W. Mayer-Gross, M.D., F.R.C.P. With foreword by Sir Russell Brain, Bt., D.M., D.C.L., LL.D. Cloth. $3.50. Pp. 96, with 9 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Cassell & Company, Ltd., 37-38 St. Andrew's Hill, Queen Victoria St., London, E. C. 4, England, 1957.

Chronische Krankheiten des Bindegewebes: Beiträge zur Pathologie und Klinik der Organ- und Systemsklerosen. Von Prof. Dr. Rolf Emmrich, Direktor der Medizinischen Klinik der Medizinischen Akademie Magdeburg. Mitarbeit von Doz. Dr. H. Petzold und Dr. J. Rott. Cloth. 41.60 marks. Pp. 280, with 51 illustrations. VEB Georg Thieme, Hainstrasse 17/19, Aufgang C, Leipzig C 1, East Germany, 1959.

Wundheilungsprobleme. Von Prof. Dr. med. Werner Block. Chefarzt der Chirurgischen Abteilung des St. Gertrauden-Krankenhauses Berlin-Wilmersdorf. Paper. 9.60 marks. Pp. 51, with 7 illustrations. Springer-Verlag, Heidelberger Platz 3, (1) Berlin-Wilmersdorf (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1959.

The Dye Injection Method for Circulatory Studies: A Critical Evaluation of the Technique, Apparatus and Results. By Walther Falholt. [Thesis, M.D., University of Copenhagen.] Scandinav. J. Clin. & Lab. Invest., vol. 10, supp. 35. Paper. Pp. 108, with 32 illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1958.

Diseases of the Colon and Anorectum. Volumes One and Two. Edited by Robert Turell, M.D., Associate Surgeon and Chief, Rectal Clinic, Mount Sinai and Montefiore Hospitals, New York City. Cloth. $35 per set. Pp. 608; 609-1238, with 634 illustrations. W. B. Saunders Company, W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

The Reticulo-Endothelial System in Growth and Tumour Formation. By Roger Wyburn-Mason, M.A., M.D., M.R.C.P. Cloth. $8; 42 shillings. Pp. 206, with 79 illustrations. Henry Kimpton (medical book department of Hirschfield Brothers, Ltd.), 134 Great Portland St., London W. 1, England; [Rittenhouse Book Store, 1706 Rittenhouse Sq., Philadelphia 3], 1958.

Surgery of the Sympathetic Nervous System. By Professor Sir James Paterson Ross, K.C.V.O., LL.D., M.S., Director of Surgical Professorial Unit, St. Bartholomew's Hospital, London. Third edition. Cloth. $8. Pp. 170, with 51 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Baillière, Tindall & Cox, 7 & 8 Henrietta St., Covent Garden, London, W. C. 2, England, 1958.

A Handbook of Medical Hypnosis: An Introduction for Practitioners and Students. By Gordon Ambrose, L.M.S.S.A., and George Newbold, M.B., B.S., M.R.C.S. Forewords by William Moodie, M.D., F.R.C.P., D.P.M., and William S. Kroger, M.D. Second edition. Cloth. $6.75. Pp. 276. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

Review of the Second Conference on Progress and Potentials in Leprosy Investigations, March 4-6, 1958, U. S. Public Health Service Hospital, Carville, Louisiana. U. S. Department of Health, Education, and Welfare, Public Health Service. Public Health Service publication no. 641. Paper. Pp. 36. U. S. Public Health Service, Washington 25, D. C., n. d.

Symposia on Child and Juvenile Delinquency Presented at the American Orthopsychiatric Association. Chaired and edited by Benjamin Karpman, M.D., Chief Psychotherapist, St. Elizabeths Hospital, Washington, D. C. Cloth. $10. Pp. 364, with illustrations by Wesley R. Wilken. Psychodynamics Monograph Series, Station L, Washington, D. C., 1959.

An Atlas of Surgery. By F. Wilson Harlow, M.B., B.S., F.R.C.S. With foreword by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D. Cloth. $8.50. Pp. 363, with 1292 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England; William Heinemann Medical Books, Ltd., 99 Great Russell St., London, W. C. 1, England, 1958.

(Continued on page 260)

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(Continued from page 250)

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RESIDENCIES AVAILABLE—IN INTERNAL MEDICINE and obstetrics and gynecology; starting July 1, 1959; excellent stipend; approved residencies; intern quota filled; write: Director of Education, St. John Hospital, 22101 Moross Road, Detroit 36, Michigan. D

GENERAL PRACTICE RESIDENCY—103 BED GENERAL HOSPITAL JCAH accredited residential suburb of Detroit; first and second year vacancies; July 1st. Cottage Hospital, 159 Kercheval, Grosse Pointe Farms 36, Michigan. D

RESIDENT PHYSICIAN—117 BED GENERAL HOSPITAL; $300 per month plus maintenance; must be graduate of AMA approved school; general services; no Exchange Visitors; July, 1959. Apply: Administrator, The Valley Hospital, Ridgewood, New Jersey. D

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(Continued on page 260)

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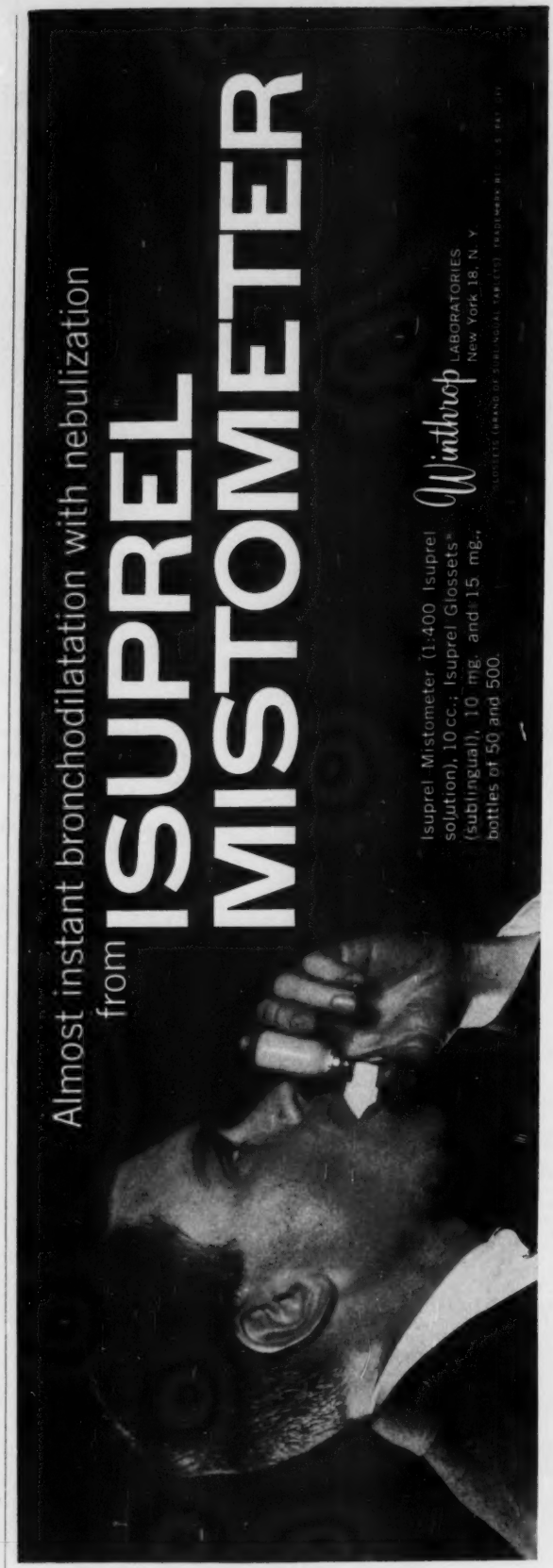
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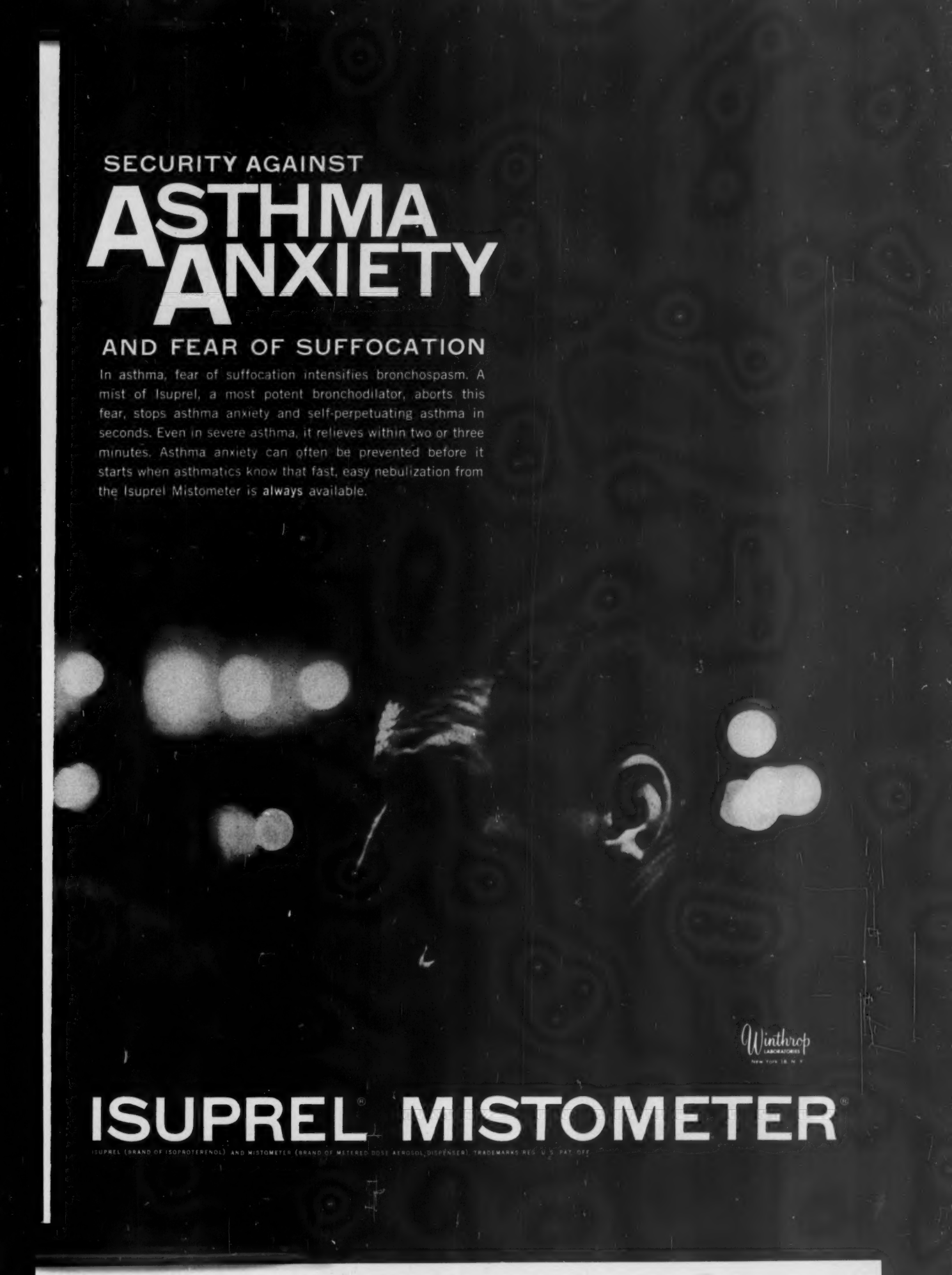
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(1) Rubin, A., and Babbott, D.: J.A.M.A. *168*:498, (Oct. 4) 1958. (2) Kinsey, A. C.; Pomeroy, W. B., and Martin, C. E.: Sexual Behavior in the Human Male, Philadelphia, W. B. Saunders Company, 1948.

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(Continued from page 257)

WANTED — LOCUM TENENS RADIOLOGIST FOR hospital department for three or four weeks November, 1959. Write: Wm. Arbonies, MD, St. Mary's Hospital, Reno, Nevada. G

PATHOLOGIST LOCUM TENENS—FOUR MONTHS TO one year board certified or lacking only the clinical year to work partly with me and partly in my absence private laboratory two hospitals: R. H. Chappell, MD, Wadley Bldg. Texarkana, Arkansas, Texas. G

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GENERAL PRACTITIONER—AGE 33; AAGP; TWO year rotating internship; post-graduate obstetrics 4 months; 5 years general practice; diplomate; licensed Pennsylvania; available now; desire partnership Pennsylvania, Ohio, New York state, Virginia, Maryland, New Jersey. Box 7422 I, % AMA.

(Continued on page 262)

(Books Received Continued)

Metabolic Factors in Cardiac Contractility. Ann. New York Acad. Sc., volume 72, art. 12. Editor in chief: Otto v. St. Whitelock. Managing editor: Franklin N. Furness. Associate editor: Marguerite Selzer. Consulting editor: Menard M. Gertler. Paper. $3.75. Pp. 387-558, with illustrations. New York Academy of Sciences, 2 E. 63rd St., New York 21, 1959.

Thank You, Dr. Lamaze: A Mother's Experiences in Painless Childbirth. By Marjorie Karmel. [Foreword by Sol T. de Lee, M.D. Assistant Clinical Professor of Obstetrics and Gynecology, University of Illinois, Chicago.] Cloth. $2.95. Pp. 190, with illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1959.

Neoplastic Disease at Various Sites. Volume II: Tumours of the Bladder. Edited by David M. Wallace, O.B.E., M.S., F.R.C.S. General editor: D. W. Smithers, M.D., F.R.C.P., F.F.R. Cloth. $11.50. Pp. 352, with 202 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

Function of the Human Body. By Arthur C. Guyton, M.D., Professor and Chairman of Department of Physiology and Biophysics, University of Mississippi School of Medicine, Jackson. Cloth. $7.50. Pp. 584, with 307 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Modern Science and the Human Fertility Problem. By Richard L. Meier. Sponsored by Conservation Foundation, 30 East 40th St., New York 16. Cloth. $5.95. Pp. 263, with illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1959.

Trauma and Disease: Selections from the Recent Literature. Edited by Alan R. Moritz, M.D., Professor of Pathology and Director of Institute of Pathology, Western Reserve University, Cleveland, and David S. Helberg, J.D. Cloth. $17.50. Pp. 903. Central Book Company, 850 De Kalb Ave., Brooklyn 21, 1959.

Die anorectalen Fisteln. Von Friedrich Stelzner, Dr. med. apl. Professor für Chirurgie an der Universität Hamburg. Cloth. 98 marks. Pp. 257, with 156 illustrations. Springer-Verlag, Heidelberger Platz 3, (1) Berlin-Wilmersdorf (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1959.

Serological Studies of Human Blood Platelets. Part 1: The Unspecific Clumping of Blood Platelets. Part 2: Platelet Antigens and Antibodies. By Jon Lundevall. Scandinav. J. Clin. & Lab. Invest., vol. 10, supp. 34. Paper. Pp. 122, with illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1958.

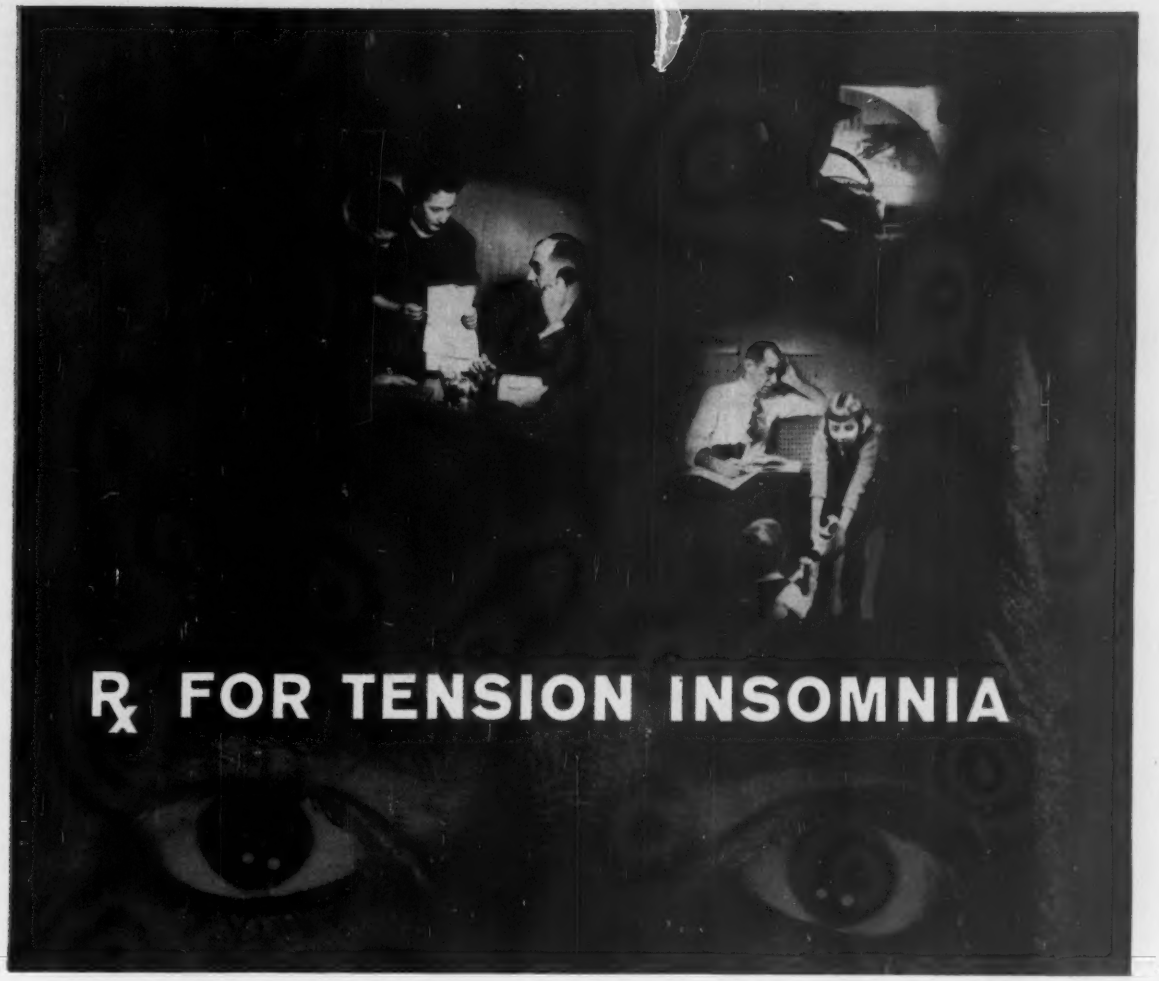
Übersicht der gebräuchlichen und neueren Arzneimittel für Ärzte, Apotheker und Zahnärzte. Von Dr. E. Bernoulli und Dr. H. Lehmann. Ninth edition. Cloth. $5.75. Pp. 555. Benno Schwabe & Co., Basel 10, Switzerland; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

Sequelae of Primary Aseptic Meningo-encephalitis: A Clinical, Sociomedical, Electroencephalographic and Psychological Study. By Ragnar Müller, M.D., and others. Acta psychiat. et neurol. scandinav., vol. 33, supp. 126. Paper. Pp. 115. Ejnar Munksgaard, Nørregade 6, Copenhagen K, Denmark, 1958.

Medicine for Nurses. By M. Toohey, M.D., M.R.C.P., D.C.H. With chapter on psychological medicine by Henry R. Rollin, M.D., D.P.M. Fourth edition. Cloth. $7. Pp. 663, with 188 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

Lesioni poliomielitiche del sistema nervoso centrale di interesse otorinolaringologico: Istopatologia e correlazioni anatomo-cliniche. Di G. C. Angela e D. Galli della Loggia. Annali di laringologia, otologia, rinologia, faringologia. Fascicolo speciale. Paper. Pp. 77, with 50 illustrations. Giovanni Capella, Via Garibaldi 1, Cirié, Italy, 1958.

(Continued on page 262)



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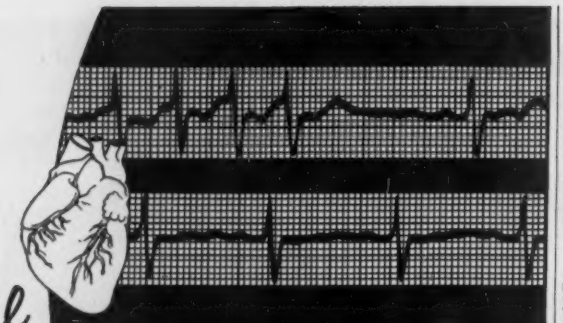

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1. Bellet, S., Finkelstein, D., and Gilmore, H.: A.M.A. Archives Internal Med. 100:750, 1957.

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(Continued from page 260)

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RADIOLOGIST — BOARD CERTIFIED; INCLUDING isotopes, age 34; hospital and private office experience; consider any area; available July, 1959. Box 8062 I, % AMA.

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INTERNIST—DIPLOMATE; PRIVATE PRACTICE AND teaching experience; additional experience allergy and hematology; desires permanent association. Box 8061 I, % AMA.

GENERAL PRACTITIONER — DESIRES TO MOVE south; Virginia or adjoining state; group or salaried position only; 36; Class A graduate; U. S. born; 11 years general practice. Box 8055 I, % AMA.

ASSOCIATION WITH GROUP, SUBURBAN OR RURAL northeastern United States; desired by general practitioner; 30; family; ambitious; available October, 1959, when military obligation complete. Box 8038 I, % AMA.

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PATHOLOGIST—37 YEARS OLD WITH OUTSTANDing and exceptionally broad clinical and anatomical background seeks relocation only because present situation lacks opportunity for advancement; will consider other opportunities as well as laboratory management. Box 7963 I, % AMA.

OBSTETRICIAN-GYNECOLOGIST — 33; BOARD ELIgible; university trained; family; experienced; excellent references; desire permanent relocation association, clinic, academic where genuine need anywhere, various licensure; details first letter. Box 7892 I, % AMA.

(Continued on page 264)

(Books Received Continued)

Leishmaniose visceral (calazar). Por J. Rodrigues da Silva. [Thesis, Professor, Department of Tropical and Infectious Diseases, National Faculty of Medicine, University of Brazil, Rio de Janeiro.] Paper. Pp. 498, with 142 illustrations. Sociedade editóra e gráfica Ltda., Rua Matipo, 115, Rio de Janeiro, Brazil, 1957.

Penicillin Prophylaxis in Obstetrics. By Olof Widholm. Ann. chir. et gynaec. Fenniae, vol. 47, supp. 75. Paper. Pp. 29, with 5 illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1958.

Hernias diafragmáticas (en el adulto y en el niño). Por Dr. Alfredo J. F. Cesanelli y Dr. Juan José Boretti. Paper. Pp. 344, with 95 illustrations. Apartado de las Actas de la Asociatión argentina de cirugía, Buenos Aires, Argentina, 1958.

Studies on Serum Lipids and Lipoproteins in Hypertension. By Eliel Waris. Acta med. scandinav., supp. 337. Paper. Pp. 79, with illustrations. Acta medica scandinavica, Stockholm K. Sweden, 1958.

Tumori orbito-paranasali (studio clinico). Di Riccardo Fregni e Attilio de Poli. Arch. ital. otol., vol. 68, supp. 33. Paper. Pp. 333, with illustrations. Archivio italiano di otologia, rinologia e laringologia, Via C. Farini 40, Milan, Italy, 1957.

Experimental Studies on Radioactive Zinc in the Male Reproductive Organs of the Rat. By Bengt Wetterdal. Acta radiol., supp. 156. Paper. 30 Swedish kronor. Pp. 83, with 37 illustrations. Acta radiologica, Box 2052, Stockholm 2, Sweden, 1958.

La cartographie thyroïdienne: Méthode cartographique et applications cliniques. Par Jean Martin. [Thesis, M.D., University of Nancy, 1957.] Paper. Pp. 313, with 112 illustrations. Société d'impressions typographiques, Nancy, France, 1958.

Studies on the Effect of Thyrotropic Hormone on the Thyroid Function in Man. By Jerzy Einhorn. Acta radiol., supp. 160. Paper. 30 Swedish kronor. Pp. 107, with 23 illustrations. Acta radiologica, Box 2052, Stockholm 2, Sweden, 1958.

Congenital Atresia of the Small Intestine: A Roentgenographic Study of 24 Cases. By H. Gladnikoff. Acta radiol., supp. 164. Paper. 25 Swedish kronor. Pp. 58, with 19 illustrations. Acta radiologica, Box 2052, Stockholm 2, Sweden, 1958.

Thrills and Regressions. By Michael Balint, M.D., Visiting Professor of Psychiatry, College of Medicine, University of Cincinnati, Cincinnati. Cloth. $4. Pp. 148. International Universities Press, 227 W. 13 St., New York 11, 1959.

Manual of Differential Diagnosis. By William C. Matousek, M.D., Chief, Medical Service, Veterans Administration Hospital, Miles City, Montana. Cloth. $8. Pp. 352. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1959.

Don't Worry About Your Heart. By Edward Weiss, M.D. Cloth. $3.95. Pp. 203. Random House, Inc., 457 Madison Ave., New York 22; Random House of Canada, Ltd., 1149 King St., W., Toronto 2, Canada, 1959.

A Guide to Nuclear Energy. By R. F. K. Belchem, C.B., C.B.E., D.S.O. Cloth. $3.75. Pp. 77, with 13 illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1958.

Young Children in Hospitals. By James Robertson. With foreword by Milton J. E. Senn, M.D. Cloth. $3. Pp. 136. Basic Books, Inc., 59 Fourth Ave., New York 3, 1958.

Die Presbyopie und ihre Korrektion. Von Sten Stenius. Acta ophth., supp. XLVII. Paper. Pp. 128, with 32 illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1958.

Davis' Gynecology and Obstetrics. Revised pages for volumes 1, 2, and 3, and supplementary index. Loose-leaf. Various pagination. W. F. Prior Company, Hagerstown, Md., 1958.

The Status and Needs of Cardiovascular Research Support in the United States. Paper. Pp. 28; 14, with illustrations. American Heart Association, 44 E. 23rd St., New York 10, 1958.

Advances in Virus Research. Volume VI. Edited by Kenneth M. Smith and Max A. Lauffer. Cloth. $10. Pp. 382, with illustrations. Academic Press, Inc., 111 Fifth Ave., New York 3, 1959.

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REFERENCES

1. Gaillard, G. E.: New York J. Med. 56:14, 1956.
2. Passenger, R. E., Spain, W. C. and Strauss, M. B.: J. Allergy 27: 409-423, 1956.
3. Fontana, V. J.: GP 10:47, 1954.
4. Gaillard, G. E.: J. Allergy 21:55, 1950.
5. Strauss, M. B. and Spain, W. C.: J. Allergy 17: 1-10, 1946.
6. Neidorff, H. A.: Personal Communication.

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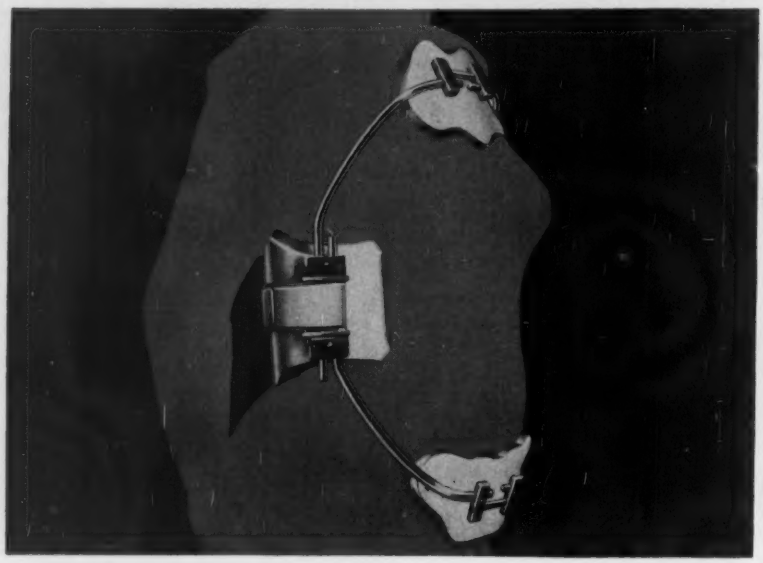

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(Continued from page 262)

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RADIOLOGIST — BOARD CERTIFIED; DIAGNOSIS and therapy; trained in a large eastern university center; desires association leading to partnership. Box 8010 I, % AMA.

UROLOGIST—COMPLETING RESIDENCY TRAINING at large charity hospital; available July; veteran; 1½ years practical experience; married; desires association with urologist or group; available for interview. Box 7978 I, % AMA.

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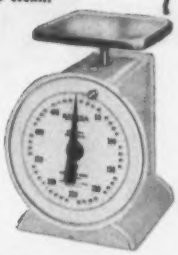

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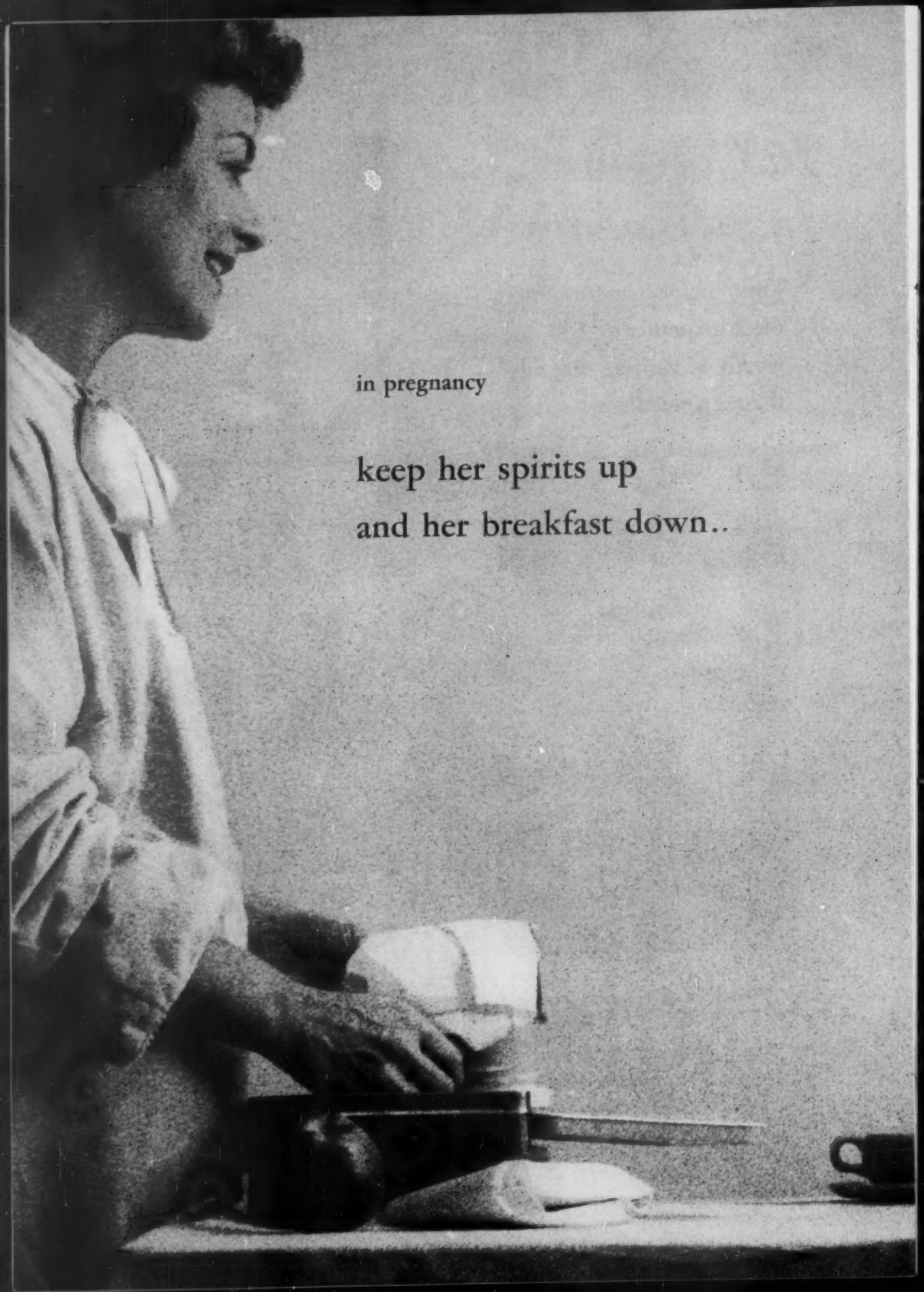
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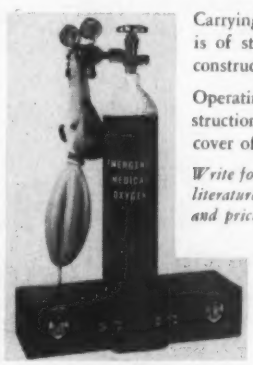

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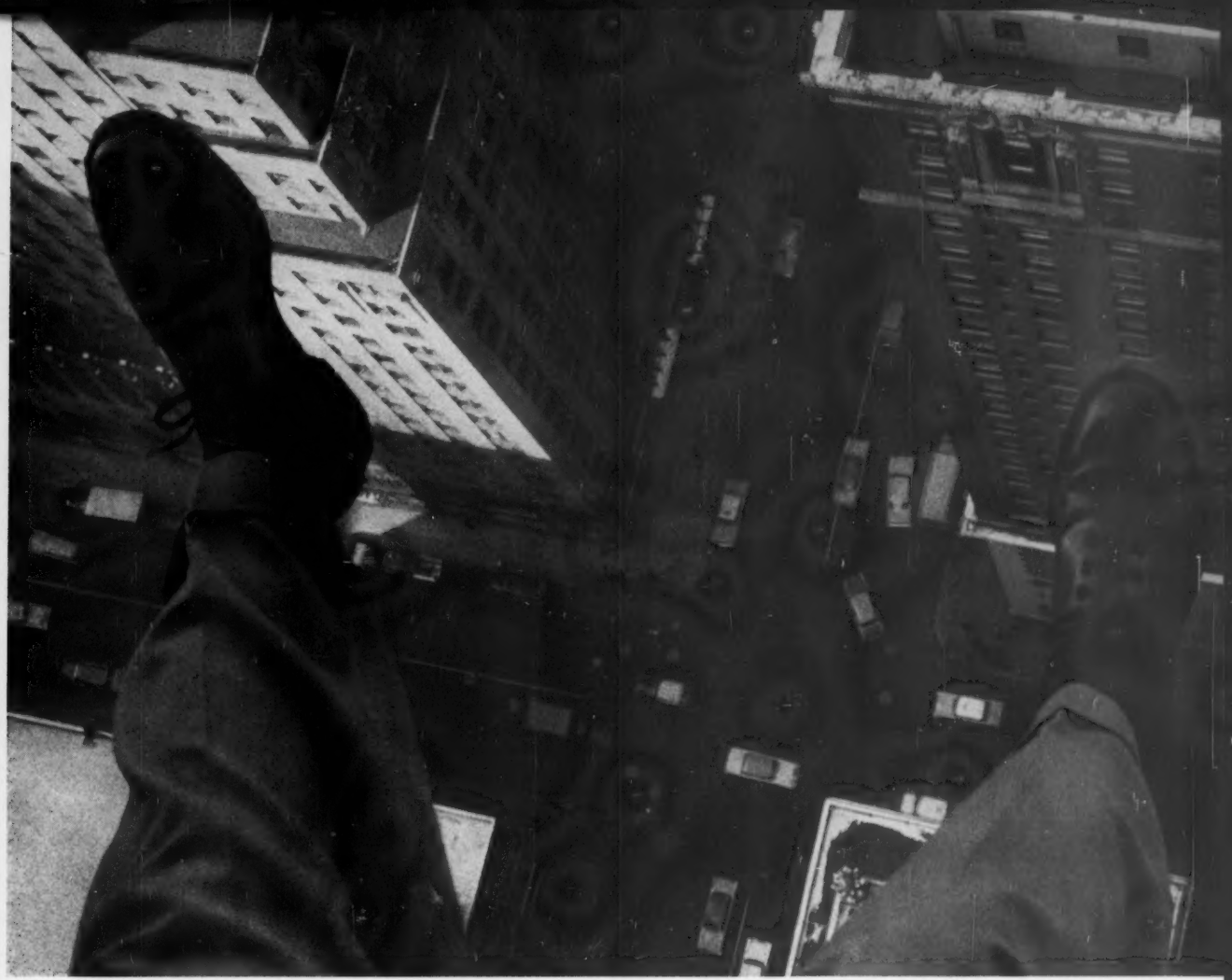

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